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THE HEART IN ANEMIA*

LAURENCE B. ELLIS, M.D.,† AND JAMES M. FAULKNER, M.D.†

BOSTON

OXYGEN transport to the tissues is dependent both on the proper functioning of the cardiovascular apparatus and on an adequate level of hemoglobin in the circulating blood. The heart and the peripheral circulation act as the propulsive and distributive forces for this function and the hemoglobin as the vehicle. Hence any marked insufficiency in the hemoglobin throws a burden on the circulatory apparatus, and this additional strain may result in clinical symptoms and signs referable to the heart and peripheral blood vessels.

Clinical observations concerning the various effects of severe chronic anemia on the heart have been made and reported many times for at least a century. For the most part these observations have dealt with a few cases only and have been concerned with the findings made during the anemic phase and not when the blood level had been restored to normal. We have therefore made clinical observations on a series of 47 patients with severe chronic anemia (hemoglobin levels varying from 8 to 57 per cent) in 19 of whom the anemia was of the hyperchromic variety, and in 28 of whom it was hypochromic. Thirty-one of these cases have also been studied when the anemia had been partially or completely relieved. None of the patients had any definite evidence of heart disease except that many of them fell into the older age group and therefore inevitably had degenerative vascular disease to a greater or lesser degree. Observations were made of the size of the heart, the occurrence of murmurs, the arterial blood pressure and electrocardiographic changes, together with signs and symptoms referable to disturbance of circulatory function, and these observations were correlated with the degree of the anemia.

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston.

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†Instructor in medicine, Harvard Medical School; junior visiting physician, Boston City Hospital.

CARDIAC ENLARGEMENT

As long ago as 1857 Bamberger[1] mentioned that cardiac enlargement might be found in conjunction with anemic conditions. Subsequently numerous observers[2–9] have found enlargement in a varying percentage of cases of severe anemia. Gautier[10] in 1899 demonstrated such an increase in size by the percussion method in 20 of 22 patients, and showed that the heart became smaller when the anemia was relieved. Ball[11] was the first to show such an increase in heart size by x-ray measurements with reduction to a normal diameter after recovery from the anemic state. Others,[12–14] have since confirmed this finding and shown that this return to a normal size may occur within a very few weeks.

We have studied the cardiac size of 38 cases of chronic anemia by teleoroentgenographic measurements. Twenty of these patients had enlarged hearts. There was a tendency for enlargement to occur more frequently in patients with particularly low hemoglobin levels. There also appeared to be some correlation between the age of the patients and the frequency of enlargement. Of the 22 patients under fifty, with an average hemoglobin level of 36 per cent, 8 showed enlargement, whereas of the 16 patients fifty or over, with an average hemoglobin level of 39 per cent, 12 showed enlargement and 4 had none. There was no relation between the type of anemia and the occurrence of enlargement. Although it is probable that the duration of the anemia and the degree of physical activity in which the patient engaged, as well as dietary deficiencies other than that which produced the anemia, may have been of importance as predisposing to cardiac enlargement, our data did not permit us to evaluate such factors. None of the patients, however, had any other clinical evidence of vitamin deficiency.

Measurements of the cardiac size both before and after successful treatment of the anemia were made in 26 cases. Eighteen of these showed a definite decrease in size of the heart shadow (varying from 1.0 to 4.7 cm. in the transverse diameter), and in 8 there was no essential change. The greater the degree of the anemia the more likely was the heart to decrease in size following improvement, which is natural since such patients were more prone to have initially enlarged hearts. The changes observed took place within a period of three to twelve weeks in most cases, although in a few cases the second observation was not made until a longer time had elapsed. In 7 of the patients with initial enlargement the heart had decreased to normal size at the time of the second observation, and the hearts of 6, though smaller, were still above the upper limits of normal. Five patients whose hearts were normal in size at the outset showed a decrease after improvement. In none of the 8 patients whose hearts remained unchanged in size was there an initial enlargement.

A third check-up of the cardiac size months or years after the second examination was made in 8 cases. Of the 3 patients whose hemoglobin level remained unchanged, one showed a further decrease in heart size. Five showed continued improvement in their blood, and in 2 of these the hearts had grown still smaller.

An important factor in aiding the return of the heart size toward normal in our patients is the fact that for the most part during the period of treatment of the anemia they were either kept in bed or lived a bed-and-chair existence on the hospital wards, whereas prior to the discovery of their anemias most of them had been engaged in a much greater degree of activity and had thus subjected their hearts to much more strain.

It is evident from the comparatively rapid decrease in size of the heart that may occur that such enlargement must be due at least in part to dilatation. Cardiac hypertrophy, however, has also been shown to take place. Cabot and Richardson[15] found from autopsy study that there was increase in heart weight in 18 of 19 patients dying of pernicious anemia. In 1 case the heart weighed 710 gm. Porter[12] observed a heart weighing 630 gm. in a man dying of hookworm anemia. Numerous experiments on animals bearing on this point have been made, the majority of which[16, 17] have given evidence of cardiac hypertrophy as the result of profound anemia. It is Porter's belief that anemia of short duration results in cardiac dilatation which can be completely overcome with relief of the anemia, but that in cases of long duration hypertrophy takes place and this can never be completely reduced. The belief of some of the older clinicians[3] that anemia may lead to permanent organic valvular disease is not now accepted.

In addition to dilatation and hypertrophy, the anemic heart muscle undergoes a form of fatty degeneration which has long been familiar to pathologists.[18, 19] The characteristic yellow streaking clearly visible on the endocardial surface has given rise to the term "tigering." These histologic changes are comparable to those observed in experimental animals subjected to low oxygen pressures for long periods.[20]

CARDIAC MURMURS

That *systolic murmurs* develop frequently in patients suffering from anemia has been recognized for nearly a hundred years,[1, 2, 4, 5, 7, 21] and is commented on in almost every textbook discussion of the causes of murmurs. Of 46 patients studied by us, 32 had systolic murmurs of varying intensity. The incidence of maximum intensity was divided equally between the pulmonic area in the second or third interspace to the left of the sternum and the apex of the heart. However, since the murmur, when intense, is often audible over the entire precordium it may be difficult to determine whether one is dealing with a single murmur emanating from the pulmonic or mitral area or with the fusion of two murmurs arising from these areas. Both murmurs are high-pitched and blowing in character.

The causative factors for the production of systolic murmurs differ according to their location. In any condition in which the velocity of blood flow is increased a pulmonic systolic murmur is common. This is true following exercise, in pregnancy and in hyperthyroidism as well as in anemia. Hence the pulmonic systolic murmur of anemia might well be associated with an increase in the velocity of the blood, although the exact mechanism of its production is not clear. The apical systolic murmur may be due to a functional mitral regurgitation secondary to dilatation. The presence and intensity of systolic murmurs in our cases were roughly proportional to the amount of cardiac enlargement and to the severity of the anemia. Nineteen of the cases were followed; in 14 the murmur became less marked or disappeared as the anemia improved. Fourteen of these cases were also followed by serial x-ray films; in 9 of the 10 in which there was a decrease in the murmur the heart size also diminished, whereas all 4 patients without change in murmur also showed no change in heart size.

Diastolic murmurs heard in conjunction with anemia are much less common than systolic, although their existence has been noted since 1861,

when Friedreich[18] first commented on the occurrence of such a murmur in a case in which autopsy subsequently proved that the valves were normal.[7, 13, 22–25] The usual diastolic murmur which is heard is early and blowing in character, and is best made out in the third left interspace near the sternal border. It is generally spoken of as aortic, and is thought to be due to functional aortic regurgitation secondary to cardiac dilatation. However, it may be that some at least of these murmurs are in reality due to a functional insufficiency of the pulmonary valve. Although Goldstein and Boas[9] report an incidence of 10 per cent of these murmurs in 39 cases of anemia, this is a very much higher incidence than that generally reported and than that which we have encountered. The murmurs occur only in association with very severe grades of anemia. The only patient in our series who exhibited a diastolic murmur of this type was a young woman of thirty-five suffering from pernicious anemia, with an initial hemoglobin level of 8 per cent and marked cardiac enlargement as judged by percussion measurements. With improvement in the anemia the murmur promptly disappeared and the heart size decreased. A check-up six years later showed the heart to be normal in every respect and the murmur to be still absent.

Presystolic apical murmurs in anemic patients have also been described,[9, 13, 26, 27] and undoubtedly do occur. We ourselves have never encountered a true presystolic crescendo apical murmur in an anemic patient which was not clearly due to organic disease of the mitral valve. It is true that one not infrequently obtains a deceptive impression of a presystolic murmur due to a booming first sound or a presystolic gallop in anemic patients as well as in other persons whose hearts are overactive. This is seen especially in thin-chested individuals following exercise and in excited persons as well as in pregnancy and hyperthyroidism.

ARTERIAL BLOOD PRESSURE

Reports[13, 14, 28, 29] concerning the effect of severe chronic anemia on the arterial blood pressure are in general in agreement that there is a tendency for a lowering of the systolic and diastolic pressures, and an increase in the pulse pressure in the milder cases while in the more severe the latter may be lowered. Of the 23 patients followed in our study 10 showed an increase in the systolic pressure of 10 mm. of mercury or over and in 14 the diastolic pressure increased 10 mm. or more following improvement of the anemia. Twice the systolic pressure decreased 10 or 15 mm., but in no case was there a significant drop in the diastolic. In 12 cases improvement was accompanied by a decrease in pulse pressure, in 8 no change occurred and in 3 there was an increase. A patient whose initial blood pressure was 125/60 had an increase to 190/115 as he improved, and in another case the pressure rose from 132/55 to 180/60.

The factors chiefly responsible for a diminution in blood pressure are a compensatory peripheral vasodilatation, decreased blood viscosity and a blood volume which, while usually within normal limits,[30] is in the lower range of normal and often less than the blood volume of the patient when his anemia has been relieved. The increased cardiac output occurring during the anemic phase tends, of course, to increase the systolic pressure, and therefore plays an important part in preventing the systolic pressure from falling even lower.

ELECTROCARDIOGRAPHIC CHANGES

Most of the published reports[12, 13, 29, 31–33] concerning the effect of anemia on the electrocardiogram conclude that no striking electrocardiographic changes are to be noted. Tung et al.[18] state that prolongation of the Q–T interval may occur, as well as other minor changes, and Elliot[34] found a flattening of T_1 in an anemic patient suffering from angina pectoris in whom autopsy showed the heart to be normal. Zimmermann[35] found that low amplitude and T-wave abnormalities were occasionally present in patients with severe anemia who had angina pectoris, but did not follow them after improvement in order to see whether the electrocardiographic changes had disappeared.

It has been observed[1] in dogs rendered acutely anemic by massive hemorrhage that at systolic-blood-pressure levels in the vicinity of 40 mm. of mercury, changes in the electrocardiogram occur which suggest an inadequate coronary blood flow, and that these changes can be promptly eliminated by raising the blood pressure through the infusion of blood or saline solution. Although in several human cases of profound shock and acute hemorrhage, in 1 of which no blood pressure was obtainable, we found the electrocardiogram normal except for tachycardia, in a number of cases of severe chronic anemia we observed electrocardiographic changes which promptly disappeared with the return of the blood toward normal.

Electrocardiograms were taken in 45 of the 47 cases in the group, and in 10 abnormal records were found. The electrocardiograms were repeated in 29 cases. Of the 7 cases in this group which were abnormal at the outset, 5 returned to normal coincidentally with improvement in the blood picture. In one of the 5 the abnormality consisted of an A-V nodal rhythm, a finding which has

been observed in experimental anoxemia.[37] The other 4 cases showed consistent changes in the T waves which could hardly be attributed to coincidence; to these we have added 4 similar cases which have come under our observation since the original study was concluded. The blood findings and corresponding electrocardiographic changes are shown in Table 1 and Figures 1 to 5.

TABLE 1. *Electrocardiographic Changes Before and After Treatment in 8 Patients with Severe Anemia.*

Case No.	Diagnosis	Age	Hemoglobin (Sahli)	Red Blood Cells	First Electrocardiogram	Subsequent Observations: Period after first electrocardiogram	Hemoglobin (Sahli)	Red blood cells	Electrocardiogram
		yr.	*%*	*$\times 10^6$*		*days*	*%*	*$\times 10^6$*	
1	Hypochromic anemia	70	36	3.4	T_1, T_2 diphasic; ST_1, ST_2 depressed; left-axis deviation.	49	88	4.45	T's normal; ST's normal; axis unchanged.
2	Hypochromic anemia	61	14	1.35	T_1 low; ST_1, ST_2 depressed.	90	66	4.14	T's normal; ST's normal; QRS voltage increased; axis further to left.
3	Pernicious anemia	84	23	1.10	T_1 low; ST_1 depressed; left-axis deviation.	90	64	4.16	T's normal; ST's normal; axis further to left.
4	Pernicious anemia	69	25	0.90	T_1 flat; T_2 low; QRS voltage low.	35	75	4.35	T's normal; QRS voltage increased.
5	Aleukemic myelosis	63	17	0.49	T_1 inverted; T_2 diphasic; ST_2 depressed.	11	25	1.30	T's normal; ST's normal.
6	Hypochromic anemia	22	17	1.03	T_1 inverted; ST_1, ST_2, ST_3 depressed.	10	59	3.37	T's normal; ST's normal.
7	Pernicious anemia	73	19	0.72	T_1, T_2, T_3 flat; QRS voltage low.	7	30	1.31	T_1, T_2 low; T_3 flat; QRS voltage low.
						14	38	3.04	T's normal; QRS voltage increased.
8	Pernicious anemia	35	8	0.40	T_1, T_2, T_3 flat; ST_2 depressed.	3	8	0.50	T_1 flat; T_2 upright; T_3 low.
						8	28	1.30	T_1 low; T_2, T_3 normal.
						12	40	1.75	T_1 flat; T_2, T_3 voltage increased.
						17	47	2.06	T's normal

The highest hemoglobin found in association with an initial abnormal electrocardiogram was 36 per cent, occurring in 1 case; in all the other cases the hemoglobin was 25 per cent or less. In the entire group there were 11 patients with initial blood levels of 25 per cent or less. Seven of these had abnormal electrocardiographic records which became normal as the anemia improved and in 1, although the record was within normal limits, there was considerable increase in voltage with improvement in the blood picture.

A fairly consistent pattern runs through these records, namely a depression of the S-T segment and flattening or inversion of the T wave in Lead 1 or both Leads 1 and 2. Although this pattern is similar to that produced by digitalis, the latter factor was ruled out in every case. The possibility of vitamin B deficiency is more difficult to exclude, since all the patients were suffering from chronic illness. However, none of them showed other signs of vitamin B deficiency, the anemias were of varied etiology, and none of the electrocardiograms exhibited the sign so frequently encountered in this deficiency, namely prolongation of the Q-T interval. Furthermore, the electrocardiographic abnormalities appeared to be related to the degree of the anemia. The transient nature of the T-wave changes indicates that they were not due to any irreversible myocardial damage, and it is quite possible that myocardial anoxia would account for them. Certain experimental and clinical studies have been made which indicate that myocardial anoxia produces changes of this nature in the electrocardiogram.[28–42] It is unlikely that cardiac dilatation alone would account for them, although in the only 2 cases with abnormal electrocardiograms in which satisfactory x-ray measurements of the heart were obtained before and after treatment, pronounced dilatation was present, as evidenced by a decrease in the transverse diameters of the heart of 2.9 and 2.3 cm. respectively. The level of hemoglobin at which myocardial anoxia occurs in an individual case logically depends on the adequacy of the coronary circulation. This would account for the tendency noted in this series for electrocardiographic changes to be found more commonly in older patients. It is possible that fatty changes in the myocardium also have an effect on the electrocardiogram. This also is presumably a reversible change, although

probably a relatively slow one, and one which would be likely to cause the improvement in the electrocardiogram to lag behind the improvement in the hemoglobin level.

CONGESTIVE HEART FAILURE

Most patients with severe anemia complain of symptoms many of which are similar to those present in persons with impending or actual heart failure. Thus, dyspnea on exertion, palpitation and dependent edema are of frequent occurrence. Of our 47 patients, 35 suffered from dyspnea on exertion of varying degree when first seen. Interestingly enough, the occurrence of dyspnea could not be correlated with the degree of anemia, nor did it bear any relation to age. In all the cases followed, the dyspnea improved markedly as the anemia was relieved. Twenty-one of our patients also had dependent edema, usually slight. The edema and dyspnea did not necessarily coexist. Ten of the 12 patients with edema who were followed were completely relieved of it as the blood level returned to normal.

ANGINA PECTORIS

Several authors[32, 34, 35, 43, 44] have commented on the occasional occurrence of angina pectoris in patients with anemia. In our present series there is 1 such case and we have encountered several others at various times. The case record of the patient in this series is as follows:

H. L., a 65-year-old English artisan, had been followed at the Boston City Hospital since 1927 for pernicious anemia. He had done well under liver treatment until August, 1931, at which time his physician told him that he had high blood pressure and hardening of the arteries and should eat no meat. He thereupon discontinued his liver and shortly thereafter began to experience increasing weakness, easy fatigue and dyspnea on exertion. Early in January, 1932, he commenced to develop typical angina pectoris, that is, squeezing precordial pain radiating down both arms, accompanied by a sensation of smothering and occurring on exertion especially in the cold air, and relieved by rest and nitroglycerin. As time went on this pain was brought on by less and less exertion. In early March there developed slight edema of the ankles and a sore tongue. The patient entered the hospital on March 21, 1932.

On physical examination the positive findings were a

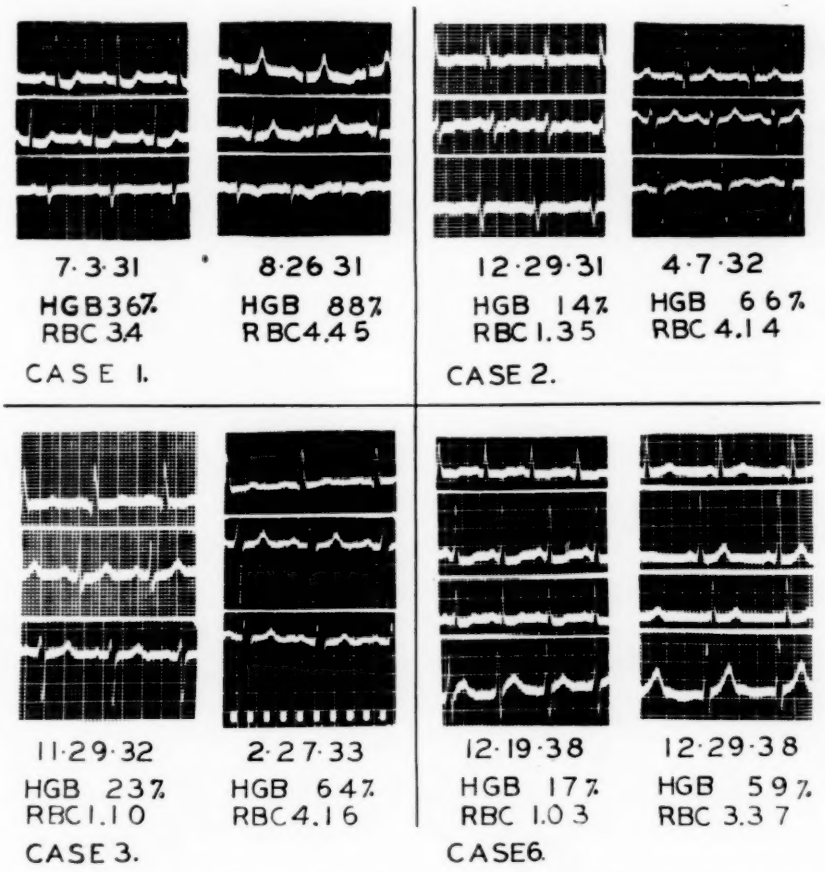

FIGURE 1. *Electrocardiograms from Cases 1, 2 and 6 (hypochromic anemia) and Case 3 (pernicious anemia).*

smooth tongue, moderate sclerosis and tortuosity of the peripheral arteries and poor heart sounds with no murmurs. The chest was emphysematous but there were no rales or abnormal breath sounds. The arterial blood pressure was 140/60. There was no edema. The hemoglobin was 44 per cent (Sahli) and the red-blood-cell count 1,550,000. A teleoroentgenogram of the heart showed it to be within normal limits, its transverse diameter being 12.1 cm. and the internal diameter of the chest 29.5 cm. An electrocardiogram was normal.

The patient was given intramuscular injections of liver extract and rapidly improved, so that on discharge, May 14, 1932, the angina was completely gone and there were no other symptoms. At this time the hemoglobin was 63 per cent and the red-blood-cell count 2,300,000.

The patient returned for a check-up on July 1, 1932 and reported that he had had no recurrence of his angina or any other symptoms. Examination of the heart showed no change. The blood pressure was 130/80, the hemoglobin 80 per cent and the red-blood-cell count 3,400,000. An electrocardiogram revealed no change from the previous one. X-ray examination of the heart demonstrated that the transverse diameter had decreased 1.3 cm. to 10.8 cm. The patient was observed once more on October 11, 1938, 6½ years after the original admission. During this interval the blood had been maintained at a normal level by liver extract, and there had been no angina or other symptoms. Examination of the heart showed no change; the blood pressure was 160/80 and the hemoglobin was 80 per cent. The electrocardiogram showed no change.

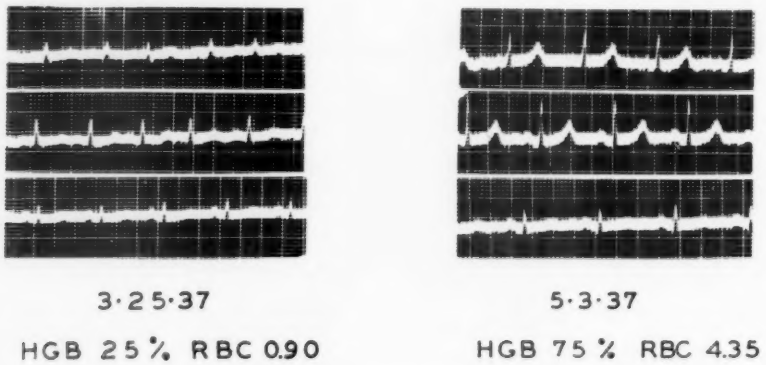

FIGURE 2. *Electrocardiograms from Case 4 (pernicious anemia).*

Since the cause of angina pectoris is generally accepted to be a disproportion between the need of the heart for oxygen and the available supply through the coronary circulation, resulting in anoxia of the cardiac muscle, it is understandable that this symptom should at times occur in patients with a profound deficiency in hemoglobin and hence in the oxygen-carrying power of the blood. In many cases of angina of this type the patient is of middle age or over and is probably suffering from some degree of atherosclerosis of the coronary vessels; hence the anemia may be considered merely to precipitate the pain in an individual who is already a potential candidate for it. However, many such patients if relieved of their anemia live for many years with no recurrence of anginal pain.

DISCUSSION

The clinical changes which have been observed to occur in the heart and circulation as the result of severe chronic anemia are all compatible with the alterations in cardiovascular physiology which are known to take place under such conditions.

Normally the oxygen-carrying power of the blood is far in excess of the requirements of the resting tissues, only one third of the available oxygen being removed from the blood in its circulation through the body.[45] It is thus apparent that, if no other compensatory forces come into play, when the hemoglobin falls to about 30 per cent of normal all the oxygen would be taken out of the blood. Actually, although there is an increased oxygen utilization in anemia,[46, 47] it is not necessary that it reach this extreme degree, for there is also a sharp rise in the cardiac output before the deficiency in hemoglobin reaches the level of 30 per cent. Observations have been made on experimental animals[48] as well as on human beings[28, 29, 46, 47, 49–51] which indicate that a progressive increase in cardiac output occurs in severe chronic anemia. The exact point at which this rise first occurs is in some dispute, but most reports indicate that it takes place at a hemoglobin level of about 50 per cent. Dautrebande[46] found in man that the cardiac output may be doubled when the hemoglobin is 30 per cent of normal and tripled when it reaches 20 per cent, although Richards and Strauss[47] did not find so sharp a rise at low hemoglobin levels.

The finding of an increased cardiac output is corroborated by the majority of the reported observations on the effect of anemia on the velocity of the circulation. While Tarr, Oppenheimer and Sager[52] and Porter[12] found very little change from

the normal, Bornstein,[53] Blumgart, Gargill and Gilligan,[54] Stewart, Crane and Deitrick[29] and Tung, Bien and Ch'u[13] all report an increase in blood velocity which appears to be proportional to the degree of the anemia.[54]

In contrast to the increases in oxygen utilization by the tissues, in the blood velocity and in the cardiac output, there is some decrease in the blood viscosity; and the circulating blood volume,[30] while usually within the limits of normal, is frequently somewhat reduced.

Two theories have been brought forward to explain the cause of the cardiac dilatation which occurs in anemia. One[55] is that it is due to increased work of the heart occasioned by increased cardiac output is the cause. Stewart et al.[29] deny that the heart in severe anemia is called on to do excessive work in spite of the increased minute-volume output. Since the work of the heart is as dependent on the level of the blood pressure as it is on the cardiac output,[56] these investigators found in their cases that, because of the lowered blood pressure, the calculated work of the left ventricle was no greater and often less during the anemic phase than at a time when the hemoglobin level was higher and the cardiac output less. It is, however, hazardous to apply their conclusions to all cases of anemia, for it should be noted that the blood-pressure changes in Stewart's cases were greater than in most of our cases with comparable changes in the blood level, and, moreover, the heart measurements of his patients were little if any increased above normal and showed very little decrease as the anemia improved. It is quite probable, therefore, that the hearts of anemic patients in whom there is comparatively little lowering of the blood pressure are obliged to do an increased amount of work, and it is possibly these hearts that are most likely to dilate.

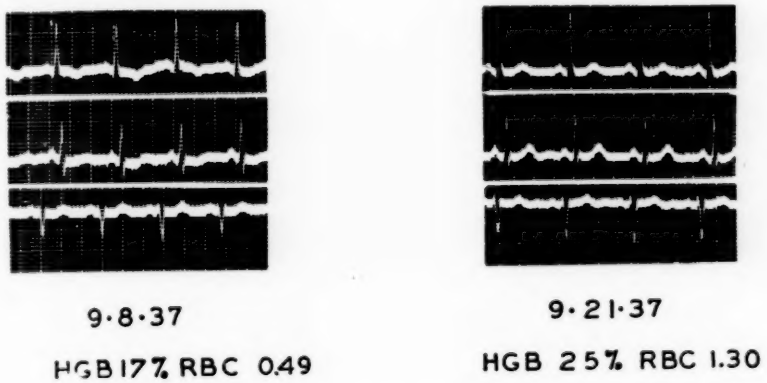

FIGURE 3. *Electrocardiograms from Case 5 (aleukemic myelosis).*

In most cases the cardiovascular symptoms of which anemic patients complain, while superficially similar to those of impending or actual congestive heart failure, are not due to primary impairment of cardiac function, and these patients do not have heart failure. The primary deficiency is in the vehicle for oxygen transport, the hemoglobin. The circulation attempts to compensate for this by a greater peripheral oxygen utilization and by an increased minute-volume output of the heart, and does sufficiently compensate so that dyspnea at rest does not occur except in the most profound cases of anemia. But with the increased demands for oxygen during physical activity this compensation breaks down and dyspnea results. Similarly, the palpitation that occurs is merely the subjective manifestation of the tachycardia which is part of the compensatory response. The edema present is usually due to a low plasma osmotic pressure caused by deficient blood proteins, and is not produced by the increased hydrostatic pressure in the capillaries which takes place in heart failure.

In primary heart failure there is not ordinarily an increase in cardiac output; in fact, the output is almost always normal or diminished, and the important factor is an inability of either the right or left side of the heart or both to expel the blood properly as it reaches it, with a resulting backing-up of the blood in the veins and capillaries of the peripheral circulation or the lungs, increase in venous pressure and loss of fluid into the tissue spaces leading to pulmonary or peripheral edema.

In rare cases, however, congestive heart failure is said to occur in patients with severe chronic anemia even in the absence of demonstrable organic heart disease. We have not encountered such a

case, but Tung et al.[13] report 6 cases. When heart failure ensues certain signs become manifest which are not present in the usual patient with anemia. These are pulmonary congestion with rales at the lung bases and the symptoms of orthopnea and cough, and peripheral venous congestion, shown by the distended jugular veins in the semi-recumbent position and enlarged tender liver and by direct measurement of the venous pressure.

Whether heart failure ever occurs in anemic patients without some additional burden or causative factor is doubtful, and difficult to determine. Tung mentions that extra physical demands such as marked physical exertion, fever and pregnancy or parturition are important precipitating factors. There are two other possible important causative factors which are difficult to evaluate. The first is the possibility that persons of middle age or over may develop heart disease and failure without a single specific sign's being demonstrable on physical examination of the heart itself or in the electrocardiogram. Hence all patients with anemia in this age group must be considered to have potential heart disease. The second point is that many patients who suffer from a severe grade of anemia, whether hyperchromic or hypochromic, are also suffering from one or more other deficiency states, because of inadequate diet or impaired gastrointestinal function. It is well known[57] that deficiency of vitamin B_1 may produce changes in the heart and circulation resulting in congestive heart failure, and hence it is not improbable that the heart failure which may appear to be due to anemia is in reality caused at least in part, by vitamin B deficiency. Indeed all the cardiovascular manifestations of anemia which we have described may in some cases, and to a greater or lesser extent, be due to the vitamin lack.

Although the physiologic effects on the circulation of primary heart failure and of anemia are thus different, the clinical symptoms and signs are frequently closely similar. Dyspnea, palpitation and edema and even angina pectoris may occur in both conditions, and in both one may find cardiac enlargement, murmurs, electrocardiographic changes and lowered blood pressure. Only too often physicians erroneously treat cases with unrecognized anemia as those of heart failure. The avoidance of such an error is of course easy if determination of the erythrocyte and hemoglobin levels of the blood is carried out, and clinically suspicion that the case is not one of true heart failure may be aroused by the absence of evidence of pulmonary and peripheral venous congestion, as shown by the lack of orthopnea and pulmonary rales and of distended neck veins in the semi-recumbent position.

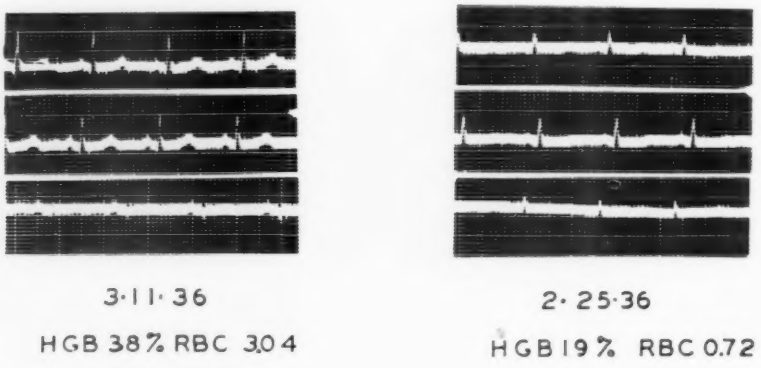

FIGURE 4. *Electrocardiograms from Case 7 (pernicious anemia).*

A far commoner mistake is failure to recognize that in the presence of heart disease even a moderate degree of anemia may precipitate cardiac insufficiency. The changes in the circulation produced by anemia add a further burden to the already inefficient and overloaded hearts of such persons with cardiac disease. Not only does the presence of anemia produce a demand on the heart for an additional output of blood at a time when the oxygen supply to the heart is less efficient than normal, but the peripheral circulatory adaptation is also overburdened. Thus the extra load on the circulation of anemia frequently is responsible for initiating congestive failure in patients with heart disease, for aggravating the decompensation and delaying recovery when once failure has occurred, and for precipitating attacks of angina pectoris. It is of particular importance to bear this fact in mind, because of all the factors which may contribute to the occurrence of heart failure, con-

gestive or anginal, anemia is one of the easiest to diagnose and one of the most amenable to treatment.

SUMMARY AND CONCLUSIONS

A study is reported on a series of 47 patients with severe chronic anemia without other evidence of heart disease. Thirty-one of these patients were followed after relief of the anemia.

Twenty of the 38 cases whose hearts were studied by x-ray showed cardiac enlargement, and of the 26 who were followed 18 showed a decrease in heart size with improvement of the hemoglobin level.

Thirty-two of 46 patients exhibited systolic murmurs. In 14 of the 19 who were followed the murmur became markedly less or absent. One patient had an "aortic" diastolic murmur which disappeared with improvement.

The anemia tended to produce a lowering of the systolic and diastolic arterial blood pressures.

Of the 45 patients studied by electrocardiogram, 10 showed abnormal records. In a group of 29 patients who were followed, 7 showed abnormal records, of which 5 became normal as the blood level increased. Four additional patients with similar abnormal electrocardiographic findings are cited. With the exception of 1 patient, all the records occurred in patients whose initial hemoglobin levels were 25 per cent or less. One abnormal electrocardiogram consisted of an auriculoventricular nodal rhythm; the remaining 8 tended to show a consistent pattern of change, namely a depression of the S-T segment and a flattening or inversion of the T waves in Lead 1 or both Leads 1 and 2.

The causation of the cardiac abnormalities is discussed and correlated with the clinical symptomatology, and with the changes in the cardiovascular physiology known to take place. It is emphasized that patients with anemia are often erroneously diagnosed as suffering from heart disease, and also that since anemia is an aggravating burden in persons with organic heart disease it is important that it be recognized and treated in such cases.

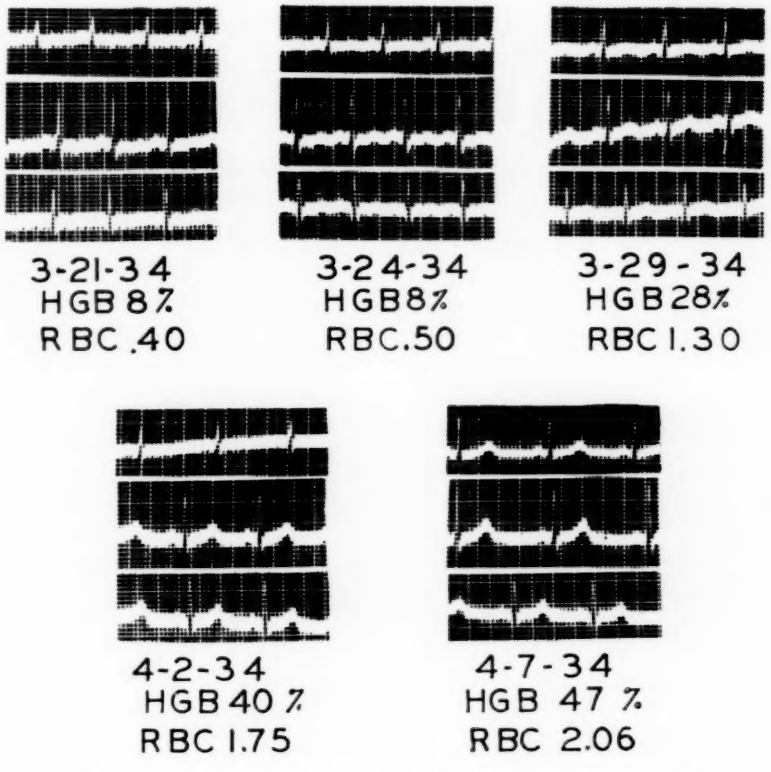

FIGURE 5. *Electrocardiograms from Case 8 (pernicious anemia).*

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DELIRIUM TREMENS: A STUDY OF CASES AT THE BOSTON CITY HOSPITAL, 1915-1936*

MERRILL MOORE, M.D.,† AND M. GENEVA GRAY, PH.D.‡

BOSTON

AT THE Boston City Hospital alcoholism is among the commonest medical diagnoses made. The number of alcoholic patients admitted is conservatively estimated at a minimal figure of 2500 per year (and may actually be 3000 cases or more§), and the expense to the City of Boston of caring for alcoholic persons is variously estimated between $500,000 and $1,000,000 per year, not counting loss of earnings due to illness associated with excessive drinking. This figure includes, of course, the cost of care in penal institutions and the handling of alcoholics by the municipal court.

Most striking among these alcoholic patients are those who suffer from delirium tremens. In the period between 1915 and 1935, 2375 persons with delirium tremens were admitted, out of 38,376 alcoholic patients (Table 1). The number varies considerably from year to year. It rose from 71 cases in 1930 to 243 cases in 1935, an increase of from 3 to 11 per cent of all alcoholic patients.

TABLE 1. *Number of Cases of Delirium Tremens Compared with All Cases of Alcoholism Admitted.*

YEAR	NO. OF ALCOHOLIC PATIENTS	NO. OF CASES WITH DELIRIUM TREMENS	PERCENTAGE
1915	523	31	6
1916	1,197	128	11
1917	1,301	155	12
1918	566	86	15
1919	564	56	10
1920	728	41	6
1921	1,322	51	4
1922	2,474	99	4
1923	2,916	140	5
1924	2,641	131	5
1925	2,057	92	4
1926	2,066	100	5
1927	2,031	113	6
1928	2,182	94	4
1929	2,092	55	3
1930	2,126	71	3
1931	2,184	146	7
1932	2,399	143	6
1933	2,291	136	6
1934	2,420	264	11
1935	2,296	243	11
Totals	38,376	2375	Average 6.2

Alcoholic cases have constituted approximately 5 per cent of all admissions to the Boston City Hospital in the last seventy years. Among all the alcoholic cases those suffering with delirium tremens constitute an average of 6.2 per cent, though this figure has risen as high as 15 per cent (as in 1918) and was 11 per cent in 1935. The sustained rise shown in the last five years is quite marked.

The increase in admissions because of alcoholism is disproportionate to the growth of the hospital, but the addition of new facilities has enabled it to care for an increasing number of alcoholic individuals.[1] The situation in Boston affecting the hospital care of alcoholic persons has been more or less unique in that no hospital has been entirely willing to accept them for care except in the most acute emergency.[2] It is of great interest to note that the trend in the incidence of alcoholic psychoses in Massachusetts as reported by Guthrie and Dayton and in New York is very similar to that exhibited by the number of admissions to the Boston City Hospital during the same period.[3]

The care of patients with acute forms of alcoholism is a heavy burden when gauged in terms of the nursing and medical attention needed, and this is particularly true when delirium tremens occurs. In this condition the danger of death is great, and the mortality is high because delirium tremens constitutes a major ordeal for the patient's entire system, accompanied or preceded as it may be by intoxication, disturbed nutrition, exhaustion and exposure of various types. Table 2 gives the number of deaths from delirium tremens compared with the total number of patients admitted with delirium tremens to the Boston City Hospital from 1915 to 1935. In this period, 2375 patients with delirium tremens were admitted and 560 (approximately 24 per cent) died. The significance of this finding may be emphasized by noting that over the twenty-one-year period included in this study, the ratio of deaths among patients with delirium tremens varied from 52 to 12 per cent, with an average of 24 per cent. During the last ten years there has been a gradual decrease in the ratio of deaths among cases of delirium tremens admitted to the hospital.

Information concerning the number of deaths

*From the Neurological Unit, Boston City Hospital, and the Department of Diseases of the Nervous System, Harvard Medical School.

This study was completed in part with the assistance of Works Progress Administration Projects (Numbers 6148-1047 and 14667) for the Study of Alcoholism at the Boston City Hospital, 1936–1938.

†Associate in psychiatry, Harvard Medical School; assistant visiting psychiatrist, Boston City Hospital.

‡Research fellow in neurology, Harvard Medical School.

§Certain alcoholic cases admitted with complications such as pneumonia, fractured skull and so forth are sometimes not formally classified as alcoholic. The variety of complications observed in patients with delirium tremens is demonstrated in Table 4, which shows the terminal causes of death.

among cases of delirium tremens compared with deaths among all cases of alcoholism is given in Table 3. Among 2015 deaths due to alcoholism at the Boston City Hospital occurring between 1915 and 1935, 560 were cases of delirium tremens. The percentage varied from 35 per cent in 1915 to 7 per cent in 1932, with an average of 28 per cent. When the deaths among cases of delirium tremens are compared with those among all cases of alcoholism, it can be seen that since 1930 the former have increased very slightly compared with the striking increase of deaths among the latter. Some features of this increase have been commented on by Dr. Timothy Leary,[4] medical examiner of the southern district of Suffolk County, who has shown that deaths due to alcoholism are also increasing in the non-hospitalized population of Greater Boston.

TABLE 2. *Deaths Among Patients with Delirium Tremens in Relation to the Total Number of Admissions of Those with Delirium Tremens.*

YEAR	NO. OF ADMISSIONS WITH DELIRIUM TREMENS	NO. OF DEATHS FROM DELIRIUM TREMENS	PERCENTAGE
1915	31	16	52
1916	128	46	36
1917	155	57	37
1918	86	24	28
1919	56	8	14
1920	41	5	12
1921	51	7	14
1922	99	20	20
1923	140	30	21
1924	131	34	26
1925	92	35	38
1926	100	31	31
1927	113	29	26
1928	94	33	35
1929	55	16	29
1930	71	16	23
1931	146	27	18
1932	143	28	20
1933	136	28	21
1934	264	37	14
1935	243	33	14
Totals	2375	560	Average 24

In the last seven years the tendency at the Boston City Hospital has been toward improvement in nursing care, which fact may well have contributed to lowering the number of fatal results among the cases of delirium tremens. A similar decrease has been noted in other clinics. Piker and Cohn[5] state that the mortality in 1910 in one reputable clinic was 37 per cent, but has decreased in the last ten years to 10 or 12 per cent through rational treatment. Since 1842, according to Chadwick,[6] deaths from alcoholism have formed a large group in records of vital statistics in Massachusetts.

In previous studies[7, 8] it was shown that men admitted to the Boston City Hospital for alcoholism outnumbered women five to one. An even greater preponderance of men is noted among cases of delirium tremens (Fig. 1). Among all alcoholic admissions deaths were commoner in the fifth decade for men and in the fourth for women. The sex and age distribution among patients dying with delirium tremens shows the greatest number of deaths among men in the same period, especially between thirty-six and forty years of age. Among women with delirium tremens most deaths occurred in the forty-one to forty-five-year age group. Among fatal cases of delirium tremens, the predominance of men over women is very striking, and should be kept in mind in any discussion of the incidence of alcoholism at the Boston City Hospital. It must also be borne in mind that the figures given can only suggest the magnitude of the problem as it is seen in the hospital, and that the numbers reported are minimal in terms of the total incidence of delirium tremens. They are only a partial index of actual conditions in the community. Even for the hospital these figures do not overstate the problem. As has been stated, many patients who are actually suffering from alcoholism are admitted because of, and are formally

TABLE 3. *Deaths Among Cases of Delirium Tremens Compared with Deaths Among All Cases of Alcoholism.*

YEAR	NO. OF CASES WITH ALCOHOLISM	NO. OF CASES WITH DELIRIUM TREMENS	PERCENTAGE
1915	46	16	35
1916	126	46	37
1917	149	57	38
1918	54	24	44
1919	34	8	24
1920	28	5	18
1921	21	7	33
1922	66	20	30
1923	103	30	29
1924	118	34	29
1925	108	35	32
1926	68	31	46
1927	80	29	36
1928	79	33	42
1929	82	16	20
1930	73	16	22
1931	118	27	8
1932	101	28	7
1933	123	28	9
1934	230	37	16
1935	208	33	16
Totals	2015	560	Average 28

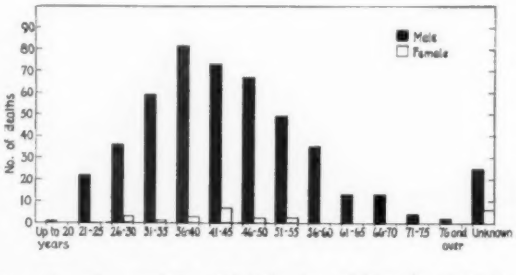

FIGURE 1. *Age and Sex Distribution of Deaths in Patients with Delirium Tremens Admitted to the Boston City Hospital, 1915–1936.*

diagnosed in terms of, the complication that occasions their admission to the hospital: pneumonia, fractures, digestive or nutritional disturbances, neuritis and so forth. For a long time many patients suffering from delirium tremens and other forms of alcoholism have been necessarily refused admission to the hospital for various reasons. Until 1917 a record was kept of these patients to whom admission was refused (Fig. 2), but since 1917

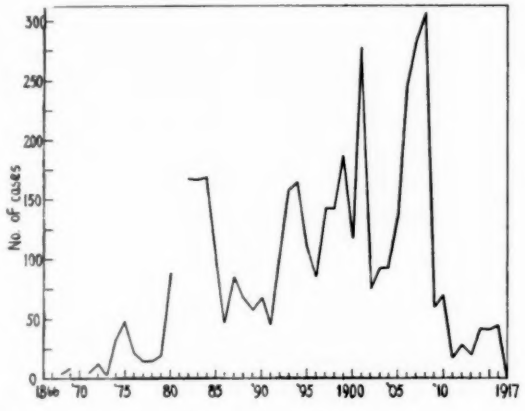

FIGURE 2. *Number of Patients Refused Admission to the Boston City Hospital on Account of Delirium Tremens and Alcoholism, 1866–1917.*

detailed information regarding their number has not been available.

Very few patients with delirium tremens die without complications (Table 4). The majority of cases in this series had serious medical and surgical conditions of which terminal pneumonia was the commonest. Dilatation of the heart was often diagnosed in fatal cases. Commonly seen, also, were conditions resulting from head injuries. Many infections occurred, with and without trauma.*

A medical problem which involves such extensive need for nursing care and medical treatment is deserving of serious consideration by municipal authorities. It is probable that cycles of increased and decreased incidence of alcoholic admissions to general hospitals will continue unless provision for more effective treatment and prevention of alcoholism is developed. It has frequently been pointed out that the alcoholic personality is distinctly a neurotic one,[13–16] and that the most effective treatment employs psychological and psychotherapeutic measures. A program in preventive medicine and public health is needed in communities faced with this problem; the basic principle of such a program must be the adequate care of the alcoholic personality in the early stages of the condition and as soon as the need becomes apparent.

No program of prevention can succeed unless there is an organized interest in the alcoholic patient as an individual, and a realization that not all such patients[16] are beyond medical assistance.

*An evaluation of the causes of death in cases of delirium tremens is difficult. However, two groups seem to stand out: those in which the cause of death was directly related to alcoholism and those in which the relation was only indirect or coincidental. Cases of pneumonia are a complication of delirium tremens although studies by Weichselbaum,[9] Grawitz[10] and others indicate that alcoholism and the associated vitamin deficiencies cause a diminution in resistance to bacterial infections.

Cases with dilatation of the heart are most frequently due to the vitamin deficiency associated with alcoholism, which has been proved to be analogous to beriberi heart disease by the studies of Weiss and Wilkins.[11] A large number of alcoholic patients die from direct involvement of the brain due either to the neuronitis, pellagra or to Wernicke's disease, both of which conditions may involve the vital centers of the brain, including the vagus region. Wernicke's disease may be recognizable grossly, particularly if the lesions are associated with hemorrhages, but this cannot be observed in all cases. In the absence of visible hemorrhage, a very experienced pathologist may recognize the bluish-gray discoloration of the periventricular tissue as suggestive of Wernicke's disease. A neuronitis of the pellagra or the beriberi type can be recognized only microscopically. Advanced neuronitis of the vagus nucleus should be accepted as a cause of death, as pointed out by Alexander.[12]

SUMMARY

Between 1915 and 1935, 38,376 patients suffering from alcoholism were admitted to the Boston City Hospital; of this group, 2375 were diagnosed delirium tremens. This figure represents a yearly average of about 250 cases or 6.2 per cent of all cases of alcoholism.

There has been in recent years a marked increase in admissions for alcoholism, and this increase has been noted as well among cases with delirium tremens. In 1930, delirium tremens cases among all alcoholic cases constituted 3 per cent and in 1935 11 per cent.

There has been a high incidence of fatal outcome among delirium cases, amounting in the period reported to 560 deaths. Although admissions of patients with delirium tremens have increased in recent years, there has been observed a marked decrease in deaths from 52 per cent in 1915 to 14 per cent in 1935. There has not been a corresponding decrease in deaths among all cases of

TABLE 4. *Principal Causes of Death Among Patients Suffering with Delirium Tremens.*

CAUSE OF DEATH	NO. OF CASES
Delirium tremens	153
Pneumonia	135
Dilatation of heart	80
Brain injuries	27
Heart injuries	24
Multiple injuries	19
Scalp wounds	10
Erysipelas	10
Septicemia	9
Pulmonary edema	6
Cellulitis	3
Ulcers	3
Burns	2
Peritonsillar abscess	2
Pulmonary tuberculosis	2
Injuries to neck	2
Postoperative hernia	1
Cholecystitis	1
Alcoholic cirrhosis	1
Bronchitis	1
Heat prostration	1
Hematemesis	1
Epilepsy	1
Streptococcal infection	1
Undetermined	65
Total	560

alcoholism in this period. In 1932, the deaths among cases of delirium tremens represented only 7 per cent of all those due to alcoholism, and has varied between this number and a high level of 46 per cent in 1926.

Men predominate among patients dying from delirium tremens at the Boston City Hospital, and are found in a higher percentage in the group suffering a fatal outcome than in the entire group diagnosed as having delirium tremens. Most of the men who died were between thirty-six and forty years of age, and the women were between forty-one and forty-five.

Many persons suffering from alcoholism and delirium tremens have been refused admission to the Boston City Hospital because of lack of facilities for their care. The proper treatment and disposal of these patients is a constant and expensive burden to the city (and the Commonwealth as well), and is worthy of a carefully planned and extensive program which would tend to prevent the serious secondary complications of alcoholism.

384 Commonwealth Avenue.

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TRANSMISSION OF ENCEPHALOMYELITIS IN THE HORSE AND POSSIBLE VECTORS IN THE HUMAN BEING*

JAMES STEVENS SIMMONS, M.D.†

BOSTON

IT SEEMS probable that equine encephalomyelitis has existed in the United States for at least a century, and possibly longer; and that it occurred in New England long before the outbreak recognized in the summer of 1938. However, information about the disease has been developed only during the last decade, beginning with the discovery of the Western type of virus by Meyer, Haring and Howitt[1] in 1930. In that year these workers investigated an epizootic of encephalitis which appeared among horses in irrigated districts of the San Joaquin Valley in California. As in our recent local outbreak, the first cases were recognized early in July. The incidence increased gradually throughout August, and reached a peak about the middle of September, when the disease appeared with explosive swiftness in every part of the valley. With the onset of cooler nights there was a rapid decrease and after November the disease disappeared. Infections occurred in California for the next two years, beginning with the hot weather in June or July and, except for sporadic cases, ending with cool weather. It was noted that communities affected in 1930 were relatively free of the disease in 1931 and 1932. During the latter years the condition spread over much of the western half of the United States. There was an increase in incidence during the later years of this epizootic, the attack rate being about 10 per cent in 1930, while in 1931 and 1932 it varied in newly infected areas from 20 to 80 per cent. Infection occurred in animals of all ages. The mortality was estimated at about 50 per cent, but it varied in different communities from 25 to 70 per cent.

Because of the failure to find evidence of obvious connection between cases, it was suspected that the disease had been spread by unrecognized carriers. Various other features of the disease suggested the possibility of insect transmission, and experimental attempts were made to transmit the disease through horse flies (*Tabanus punctifer*), but with negative results.

Isolation of Western Type of Virus. The California workers[1–6] isolated a filterable virus which differed immunologically from the virus of Borna disease, and from the virus of poliomyelitis, which was epidemic in California at that time. They also

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†Lieutenant colonel, Medical Corps, United States Army, Headquarters First Corps Area, Boston.

described the pathologic lesions of the disease, and suggested the term "equine encephalomyelitis."

Location of Virus in Horses. These and later studies indicate that in infected horses the concentration of infective virus is greatest early in the disease. Virus was recovered from the cerebrum, pons, medulla oblongata and spinal cord, but not from the liver, spleen or kidneys. It has also been obtained from spinal fluid, and from the cardiac and peripheral blood during the febrile period, but rarely after the development of neurologic symptoms.

Susceptible Experimental Animals. Using various methods, including cutaneous and intranasal inoculation, the virus has been transmitted to various animals, including horses, mules, guinea pigs, white mice, white rats, rabbits, monkeys and gophers. As a rule the mortality is higher in young animals, and the most valuable diagnostic animals are young guinea pigs and white mice. In 1933 Giltner and Shahan[7] observed that sheep, dogs and cats were resistant; that calves developed the disease, but some recovered; also that after intracerebral inoculation pigeons died in three days, while white Leghorn chickens were resistant. They suggested that calves and pigeons might be concerned in the epizootiology of the disease in nature. This possibility is strengthened by the work of Fothergill,[8] who has isolated the Eastern type of virus from a naturally infected pigeon obtained in the region of the recent epizootic in Massachusetts.

Eastern Type of Encephalomyelitis. During the summer of 1933 a disease resembling the California epizootic was recognized among horses in Virginia, Delaware, New Jersey and Maryland. The clinical symptoms and seasonal distribution were much the same, and the virus was pathogenic for the same species of laboratory animals. However, as has been shown by Ten Broeck and his associates,[9, 10] this disease, which was designated as the Eastern type of encephalomyelitis, differed as follows: its virus was immunologically distinct; its mortality was higher; and unlike the Western disease it was most prevalent in regions near salt marshes. Others who contributed to our knowledge of the Eastern type include Records and Vawter,[11–13] Giltner and Shahan[7] and others.

Experiments in Transmission by Mosquitoes. Prior to 1933, nothing definite was known about the transmission of equine encephalomyelitis. However, its epidemiology presented features suggesting that insects might be a factor. These included the seasonal distribution of the disease, its tendency to occur near waterways and swampy lands, its greater prevalence in rural areas among animals kept in pasture at night, and the lack of evidence of contact between individual cases. Records[14] noted that while the disease could be transmitted experimentally by intranasal instillation, normal horses stabled with infected ones did not contract the disease through contact, or through eating or drinking from the same containers.

During 1933, Kelser,[15] working in the laboratories of the Army Medical School in Washington, discovered that the virus of the Western type of the disease could be transmitted from infected to normal guinea pigs and to horses through *Aedes aegypti.*

In the spring of 1934, other workers at the Army Medical School (Simmons and Reynolds[16]) incriminated *A. albopictus,* which is a common Oriental mosquito and also breeds in houses. This work was done with a colony of *A. albopictus,* started from eggs shipped from Manila and maintained at the Army Medical School for teaching and experimental purposes. While this mosquito is not indigenous here, it is an effective vector of dengue fever and yellow fever, and its incrimination as a transmitter of equine encephalomyelitis may be of practical importance in Oriental countries.

Later in 1934, Merrill, Lacaillade and Ten Broeck[17] reported transmission of both the Western and Eastern type of viruses by *A. sollicitans,* and of the Eastern type by *A. cantator.* These are salt-marsh mosquitoes, both of which have been found in Massachusetts (Davis,[18] 1938).

Early in 1935, Madsen and Knowlton[19, 20] in Utah transmitted the Western type of virus through *A. nigromaculis* and *A. dorsalis,* and later that year Kelser[21] in New England incriminated *A. vexans.* During 1938 Kelser,[22] working at the laboratory of the Army Medical Research Board in Panama, transmitted Western virus with *A. taeniorhynchus.*

The detailed mechanism of the transmission of the virus by these mosquitoes still requires much study. The work of Merrill and Ten Broeck[23] with *A. aegypti* indicates that to ensure transmission the normal mosquitoes should feed on the infected animal early — or as soon as the animal's temperature reaches 40.5°C., which usually is from eighteen to thirty hours after its infection. After an incubation period of four or five days the mosquito can transmit the virus by biting, and it remains infected throughout its life. Actual tests were made up to three months after infection.

Working with *A. sollicitans,* Merrill and Ten Broeck[24] reported that this mosquito was first able to transmit the disease seven days after feeding on suspensions of infected guinea pigs brains, eleven days after feeding on infected guinea pigs and twenty days after feeding on an infected horse.

These workers also proved that when normal *A. aegypti* were fed with suspensions of macerated infected ones, virus was transmissible directly from one mosquito to another through seventeen passages and probably indefinitely. This may have epidemiological significance.

These preliminary studies implicate eight species of Aedes mosquitoes as potential vectors of encephalomyelitis, and it seems probable that additional species of mosquitoes and other insects are also concerned in the natural spread of the disease. In this connection, the recent (1936-1937) discoveries of Syverton and Berry[25–27] are of great interest. They have shown that *Citellus richardsonii*, the gopher or Richardson ground squirrel of the Northwest, is susceptible to the Western type of virus; also that the tick (*Dermacentor andersonii*) may serve as a vector of this virus, which survives in it through all stages of the developmental cycle, including the egg, and has been transmitted by larvae nymphs and adult ticks from infected to normal guinea pigs and gophers.

Thus, in considering the question as to the spread of encephalomyelitis in nature we are confronted with an abundance of known potential vectors, including at least eight species of Aedes mosquitoes and one species of tick. Undoubtedly other vectors will be incriminated. We have no exact knowledge concerning lower animal reservoirs of virus, but the available experimental data indicate the need for an extensive investigation of many species of domestic and wild animals and birds.

Because of the unusual prevalence of mosquitoes in New England during the summer of 1938, it is suspected that one or more of the species present were responsible for the epidemic of encephalomyelitis. However, this has not been proved. Adequate information concerning the relative prevalence throughout the year of the different species normally present in this region is not yet available. Furthermore, in no case has the virus been demonstrated in trapped mosquitoes.

It therefore appears that before one can intelligently discuss the transmission of this disease either among horses or in man, much fundamental investigation must be done.

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REPORT ON MEDICAL PROGRESS

TUBERCULOSIS

DONALD S. KING, M.D.*

BROOKLINE

THE following subjects have been selected as worthy of comment in a brief review of the important and practical advances in the study of tuberculosis that have been reported during the current year: the present status of the tuberculosis problem in Massachusetts; the importance of searching the gastric contents for tubercle bacilli; the frequency of tuberculous infection of the bronchi and trachea and the results of such infection; the problem presented by latent or asymptomatic tuberculosis with positive x-ray but no symptoms; pulmonary tuberculosis as an occupational hazard in student nurses and medical students; non-caseating tuberculosis — is it the same as "sarcoid disease"? recent attempts at statistical evaluation of the results of compression therapy; extrapleural pneumothorax — the newest surgical measure for treating pulmonary tuberculosis; vitamins in the treatment of pulmonary tuberculosis; and the use of sulfanilamide in experimental tuberculosis.

THE TUBERCULOSIS PROBLEM IN MASSACHUSETTS

The death rate from pulmonary tuberculosis in this state continues to fall. In 1937 it was 40.0 per 100,000 population; in 1938 it was 34.9. There are now 4472 sanatorium beds for the treatment of this form of tuberculosis, and for the first time there is no material delay in the admission of the patients to any of the county or state institutions. This is a source of great satisfaction, because regardless of our feelings about socialized medicine in general it is evident that public funds must be used if we are to isolate the open cases of pulmonary tuberculosis which are spreading the disease, and give the patients in the favorable stages the necessary sanatorium treatment.

TUBERCLE BACILLI IN GASTRIC CONTENTS

The importance of the search of the fasting gastric contents for tubercle bacilli was again called to the attention of the medical profession in papers by Stadnichenko and Cohen[1] and Gourley[2] at the meeting of the National Tuberculosis Association in 1937. It is surprising that these investigators should so often find tubercle bacilli in the gastric contents of children with the apparently benign childhood type of the disease. Since the publication of these papers examination of the gastric contents has become a routine in many sanatoriums in the study of cases not raising sputum. Again the number of positive reports is surprising. In the recent edition of *Diagnostic Standards* the National Tuberculosis Association insists that a patient is not to be classified as "apparently cured" until, "in case there is no sputum, the fasting gastric content has been obtained and thoroughly examined."[3]

There is one possible error in this procedure; namely, that harmless acid-fast bacilli may be mistaken for tubercle bacilli. However, guinea-pig inoculations have shown that this mistake occurs in only a small percentage of cases.

TRACHEOBRONCHIAL TUBERCULOSIS

In the entire field of pulmonary disease one of the most important advances in the last twenty years has been the recognition of varying degrees of bronchial obstruction and its effect on that part of the lungs supplied by the bronchus involved. Three degrees of bronchial obstruction can be recognized clinically if we remember that the normal bronchus widens on inspiration and narrows on expiration: an obstruction so slight that it allows air to enter easily on inspiration but impedes its flow on expiration, causing a wheeze; an obstruction which allows air to enter on inspiration but completely closes the bronchus on expiration and thus traps air in the portion of the lung supplied by that bronchus (obstructive emphysema); a complete obstruction of the bronchus which does not allow any air to enter and results in atelectasis of the lung.

All three degrees of bronchial obstruction are found in pulmonary tuberculosis. Bronchoscopic examination shows that the obstruction in such cases is due to a tuberculous process in the bronchi themselves.[4, 5] This process may be a discrete, shallow ulcer; hyperplastic granulation tissue; fibrostenosis, which is the healed stage of the foregoing processes; tuberculoma resembling a tumor; or obstruction by a tuberculous gland pressing on the bronchus or ulcerating through its wall. Bronchoscopists estimate that in 10 per cent of all cases of pulmonary tuberculosis there is an associated tuberculosis of the bronchi. Occasionally the tuberculous infection is limited almost entirely to the

*Associate in medicine, Harvard Medical School; associate physician, Massachusetts General Hospital.

bronchi. Tuberculosis carriers with positive sputum but little x-ray evidence of pulmonary tuberculosis fall into this class.

The symptoms of advanced tuberculous bronchitis are wheezing, marked dyspnea, distressing paroxysmal cough, difficulty in raising sputum and fever and malaise caused by retained secretion. Increasing cough and expectoration may be the result of bronchiectasis[6] which has developed in the area beyond a partial obstruction.

Tuberculosis in the bronchus also plays a part in the formation and persistence of pulmonary cavities. Giant or "tennis-ball" cavities[7] are frequently caused by a tuberculous process partially obstructing the bronchus and acting as a ball valve which allows the entry but not the exit of air, and thus produces a "tension" or positive-pressure cavity. These cavities may be very difficult to close by artificial pneumothorax or thoracoplasty. Even if the cavity is closed, the sputum may remain positive because it comes from the infection in the bronchus itself.

When there is complete atelectasis of one lobe or an entire lung without evidence of tuberculosis in the remaining portion of the lungs, x-ray diagnosis is difficult. In such cases a mistaken diagnosis of bronchiogenic carcinoma is sometimes made.

Bronchial tuberculosis, like tuberculous laryngitis, may heal spontaneously, but if it is extensive enough to be recognized clinically the prognosis is usually unfavorable. Emphasis is therefore being placed on the early diagnosis and treatment of this complication. So far no satisfactory treatment has been devised but such procedures as the following are being tried: deep x-ray therapy, general ultraviolet light treatment, and local treatment through the bronchoscope with silver nitrate, live wire cautery, electrocoagulation,[8] localized ultraviolet light[9] and mechanical dilatation of stenosed bronchi. In special cases tuberculomas and glands which have ulcerated into the bronchus have been removed through the bronchoscope.

LATENT OR ASYMPTOMATIC TUBERCULOSIS

It is now customary to x-ray the lungs of large groups of supposedly well people or of those with indefinite symptoms. There are few more difficult problems in medical practice today than the clinical evaluation of such x-ray films. Serial x-rays may show progression of a tuberculous process for months or years before symptoms develop. There is not even elevation of temperature, so that the old idea that the activity of a tuberculous process can be determined by the thermometer has long since been discarded. Some of these latent lesions develop into manifest or fatal disease; others clear without giving symptoms and become the scars and calcifications so common at autopsy. How, then, shall we select the cases needing treatment in the asymptomatic phase?

An unusually clear and practical discussion of this problem was presented by Amberson[10] at the meeting of the Massachusetts Medical Society in June, 1938. "Sound judgment," he said, "depends on a careful correlation of all factors which can be identified and estimated in the individual case." He pointed out the dangers of infection in the adolescent girl, in the Negro race and in people of low social economic status with exhausting occupations. He stressed the importance of recency of contact in infancy and during or shortly before adolescence. "The intensity of the tuberculin reaction is no indicator of the probable behavior of latent lesions," but "long-standing allergy" as shown by the tuberculin test "is associated with an increasing relative immunity against the tubercle bacillus." Contrary to repeated statements by eminent authorities, he maintained that a first infection beyond the age of childhood should be treated with the same care as a reinfection at these ages. Multiple or larger lesions demonstrated by x-ray, he asserted, were of more significance than single or small ones; basal lesions were no more important than apical ones.

If we can rely on blood studies to tell us whether or not a given lesion is active, white-cell counts, differential counts and red-cell sedimentation rates should be of particular help in the study of asymptomatic lesions. Unfortunately, as Amberson points out, "normal findings do not exclude the possibility that a latent lesion is dangerous or even actively progressive." Nevertheless, abnormal findings in the blood are important and should be considered in the decision as to treatment. There is a danger in overemphasizing their significance.

TUBERCULOSIS IN NURSES AND MEDICAL STUDENTS

Attention is being focused on the number of cases of pulmonary tuberculosis developing in college students, medical students and student nurses.[11] The subject was considered of sufficient importance to give it a place on the program of the general assembly of the Congress of American Physicians and Surgeons in Atlantic City in May, 1938; the paper was by Soper and Amberson.[12] The percentage of positive tuberculin reactors, they reported, is higher in the East than in the Middle West and in the city than in the country. Studies made in eighty-five colleges reveal that on admission from 30 to 50 per cent of the students have positive tuberculin tests and at graduation from 35 to 60 per cent. In the medical schools on admission from 60 to 70 per cent of the students have positive tests and at graduation from 85 to

95 per cent. In the nursing schools in this country about 60 per cent have positive tests on admission and 90 per cent at the end of a three years' course of training. These figures show how quickly medical students and nurses are infected by tubercle bacilli.

When routine x-ray examinations are made, 0.6 per cent of the college students show true pulmonary tuberculosis. In the medical schools 1.5 per cent of the students give x-ray evidence of pulmonary tuberculosis on admission and an additional 1.5 per cent develop it during the four-year course. Only about half of the students in these two groups are treated for active disease. Figures for the nursing schools are somewhat higher, especially where tuberculosis wards are connected with hospitals. In the United States from 3.0 to 6.0 per cent of the student nurses have x-ray evidence of disease, and about half of them require treatment. These figures are disturbing but not alarming, for by improvement of the nursing technic the number of students developing x-ray evidence of the infection in one school was reduced from 5.5 to 1.6 per cent.

One other interesting problem which is being settled by such studies is that of the immunity conferred by slight degrees of tuberculous infection. In the nurses it has been possible to determine whether the individual giving a positive tuberculin test is less likely to develop pulmonary tuberculosis after exposure on the wards than the one who has a negative tuberculin test. The figures now obtained in this country support those published a number of years ago by Heimbeck, of Oslo, and there seems little doubt that tuberculous infection sufficient to give a positive tuberculin test affords a certain amount of immunity. Heimbeck's figures, quoted by Soper and Amberson,[12] are as follows: of 625 student nurses with positive tuberculin tests who nursed patients with active pulmonary disease, 20 developed pulmonary tuberculosis and there were no deaths; of 280 negative reactors, 57 developed pulmonary tuberculosis and there were 10 deaths. Heimbeck draws the conclusion that tuberculin allergy is tuberculin immunity.

If girls under twenty are to be allowed to nurse tuberculous patients strict precautions must be taken, but to observe the same precautions as in the nursing of scarlet fever patients seems unnecessary. All general hospitals admit some patients with pulmonary tuberculosis, usually before the diagnosis is made, and the nurse may be caring for an open case without knowing it. For this reason certain hospitals are now requiring a routine chest film on all patients admitted.

NON-CASEATING TUBERCULOSIS AND SARCOID DISEASE

Strangely enough, three groups of specialists working in different fields have "discovered" a disseminated disease occurring in the lungs and many other organs of the body which is histologically and roentgenographically like tuberculosis but runs a comparatively benign course. Tuberculosis specialists have spoken of "cold" tuberculosis, chronic miliary tuberculosis, torpid forms of disseminated tuberculosis and hematogenous non-miliary pulmonary tuberculosis. Dermatologists have found that "sarcoid disease" of the skin is histologically like non-caseating tuberculosis and that it is frequently associated with glandular enlargements and cystic bone changes. The chest x-rays of these cases often show enlarged hilus glands something like Hodgkin's disease, miliary lesions indistinguishable from miliary tuberculosis or a combination of glandular and parenchymal lesions. Ophthalmologists now recognize a form of uveitis[13] clinically resembling tuberculosis of the eye but often associated with parotitis, and accompanied by a negative reaction to strong dilutions of tuberculin rather than the expected positive reaction to very weak dilutions. This tuberculin anergy is present in most of the cases of the phthisiologist and also the dermatologist.

In the past year Pinner[14–16] has reviewed the extensive literature on these conditions and presents a sound argument that they are all forms of non-caseating tuberculosis. He maintains that if the lesions could be studied very early tubercle bacilli would be found, but that because of some peculiarity of the infecting organism or the resistance of the host, the atypical "cold" lesions develop rather than the characteristic lesions of tuberculosis. Furthermore, he cites a case of sarcoid disease which after many years of observation changed into true caseous tuberculosis. In a series of cases observed by Hunter at the Massachusetts General Hospital, however, both the glandular and miliary lesions disappeared after a few months of general hygienic care.

Typical chest x-rays of sarcoid disease may occur with erythema nodosum and rheumatic fever. This is of interest because erythema nodosum has been considered a form of tuberculosis. Five per cent of the nurses in Heimbeck's series quoted above developed erythema nodosum in the course of their training.

From the standpoint of prognosis it is important to realize that there is a group of diseases which may be confused with lymphoma or miliary tuberculosis, possibly representing an atypical form of tuberculous infection, and as a rule benign.[17, 18]

STATISTICAL EVALUATION OF COLLAPSE THERAPY

In the last ten years a great change has taken place in the treatment of pulmonary tuberculosis. In the eastern part of this country, at any rate, those well qualified to judge believe that about 70 per cent of the patients in the sanatoriums should be treated by artificial pneumothorax, phrenic nerve paralysis or thoracoplasty. However, statistics to support this strong clinical impression have been difficult to obtain, and we now have the statistician Drolet[19] maintaining that "most of such studies have limited themselves to the immediate results of treatment and are an incorrect or incomplete measure; they should deal rather with the ultimate results." He concludes: "Sanatorium or surgical treatment of pulmonary tuberculosis would seem so far to have had little effect upon the case fatality rates of the entire tuberculous population in the communities studied." "Case fatality rate" means the ratio of deaths in a given community to the new cases reported in that community during the same period of time. For example, in Massachusetts in 1915 there were 8046 new cases reported, with 4194 deaths. In 1935 there were 3594 new cases, with 1814 deaths. The case fatality in 1915 was therefore 52 per cent and in 1935 had dropped to only 50 per cent. He goes on to analyze the figures relating to cases discharged from the sanatoriums in the United States, and shows that in 1925 the mortality ratio to the total discharges alive or dead was 20 per cent, while in 1934 it was 24 per cent. He states: "It may, therefore, be concluded from the obvious decline of tuberculosis and the comparatively slight change in the case fatality rate that the preventive aspects of isolation in tuberculosis hospitals have been far more effective than those arising from sanatorium or medical treatment." The proportion of all tuberculosis cases which are now isolated in sanatoriums has increased remarkably in the past twenty years. For instance, in the state of New York in 1915 only 8 per cent of the total tuberculosis cases were isolated in hospitals, whereas in 1934 the figure had reached 34 per cent.

Drolet's only conclusion in favor of collapse therapy is that "persons dying from tuberculosis now are slightly older [3 to 5 years] than formerly."

The clinician is somewhat mystified by these indirect conclusions but is forced to reckon with them. Perhaps it is true that collapse therapy in the far-advanced cases which make up so large a percentage of the sanatorium population will prolong life but not greatly influence the mortality rate. In that case greater emphasis should be placed on early diagnosis and treatment, and we are again faced with the problem of the asymptomatic lesion. In any event, no physician who has followed carefully a large group of cases treated with collapse therapy will be willing to give up the procedure because of Drolet's figures.

EXTRAPLEURAL PNEUMOTHORAX

New methods of collapse therapy and changes in the technic of the older methods are constantly being introduced. During the past year attention has been drawn to extrapleural pneumothorax.[20–22] In many cases it is impossible to establish a satisfactory intrapleural pneumothorax because the visceral and parietal pleurae are adherent. In some of these cases the surgeon can remove a section of a rib and strip the parietal pleura from the chest wall, allowing the collapse of the underlying lung. This collapse can then be maintained by injections of air between the chest wall and the parietal pleura using the method employed to inject air between the visceral and parietal pleurae in intrapleural pneumothorax. If the patient's condition allows thoracoplasty most surgeons prefer it; if not, extrapleural pneumothorax can be established with a minimum of shock. This treatment may be sufficient in itself or may improve the patient's condition so that thoracoplasty can be performed later.

The possible complications of extrapleural pneumothorax are tuberculous infection in the extrapleural space, and rupture of a large tuberculous cavity into it as a result of the separation of the lung from the chest wall. As in all collapse treatment, there must be a rigid selection of cases, and the surgeon should not be pushed into operation "just because there is nothing else to do."

VITAMIN THERAPY IN PULMONARY TUBERCULOSIS

Many years before the present vitamin craze, cod-liver oil proved its value in the treatment of tuberculosis, and in recent years vitamins D and C have been used extensively in the treatment of intestinal tuberculosis. Many people think that it is the vitamin and not the accompanying ultraviolet light treatment which is responsible for the improvement in these cases. In recent studies of vitamin C it has been found that tuberculous patients have a very low urinary excretion of this substance. As a result, many institutions have given their patients concentrated vitamin C. No conclusive articles have appeared to date, but there seems little doubt that in an appreciable number of cases it does increase the appetite and therefore helps in the essential upbuilding process.

SULFANILAMIDE IN EXPERIMENTAL TUBERCULOSIS

At a time when sulfanilamide is being used so extensively in the treatment of various bacterial

infections it is right that its effect should be tested in the laboratory on the growth of tubercle bacilli in the test tube and in animals. Experiments to date indicate that in certain concentrations sulfanilamide does exert an inhibitory effect upon such growth.[23–25] There are as yet no reports on the use of the drug in tuberculosis in human subjects.

Sulfapyridine, too, is being subjected to the same laboratory test and experiments are under way to produce a form of sulfapyridine which can penetrate the fatty capsule of the tubercle bacillus. Needless to say, the time has not yet come to use these drugs on cases of tuberculosis occurring in general practice.

1101 Beacon Street.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25231

PRESENTATION OF CASE

A fifty-year-old female Negro nurse was admitted complaining of fever, generalized aching and sore throat of three weeks' duration.

For the past fifteen years the patient had had occasional attacks of very severe pain in the right upper quadrant, sudden in onset, requiring opiates for relief and associated with nausea and vomiting. They lasted about two days and were followed by tenderness and weakness. There was no jaundice. They recurred about every six months, the last being one year before entry. For the past seven years she had had aching and stiffness in various joints, often localized in the hands and occurring in wet weather. Three years before admission she was admitted to an outside hospital for "double pneumonia" and acute rheumatic fever, remaining there for three months. Following this she had frequent dry cough throughout the winter. Three weeks before entry she was awakened with a severe shaking chill and definite malaise. The chill lasted about ten minutes and the temperature rose to 104°F. She had slight headache. Her physician stated that she was ill with a "bad heart" and gave her digitalis. There was generalized aching, a sore throat and sore mouth. Her temperature remained at 101 to 103°F. for three days then fell to under 99.5°F. for ten days. After the acute illness she complained of great weakness though her appetite was excellent. Eight days prior to admission her temperature rose to 100°F. and she complained of gas in her abdomen. There was distention relieved by heat and an enema. She began having two or three bowel movements daily, with well-formed brown stools. She also noted pain under both shoulders and severe pain across the upper anterior chest which was not increased by respiration. Associated with this was rapid heart action. At about the same time drowsiness developed and on one occasion she complained of numbness throughout the right side of the body, except the face, which lasted for only a few hours. There was no paralysis, and complete recovery ensued. A severe dry cough developed. Back pains were noted and slight tenderness in the right wrist. Two days later anorexia developed accompanied by frequent gas pains. An enema gave good results and relief. Two days before entry her temperature was 102°F. and her sore throat seemed to be returning. On the following day her abdominal distention was again relieved by heat and an enema. Her physician found a negative abdomen, the chest clear, but a temperature of 101°F. She had had no urinary symptoms and her urine had been light colored. There had been no jaundice. She had had two children and one miscarriage.

Physical examination showed an obese, perspiring, restless woman obviously ill and in a semistuporous condition. There were frequent attacks of dry, brassy coughing. Examination of the fundi oculi was negative. The tongue was red in the center, the sides were coated. The anterior tonsillar pillars showed a dusky redness covered with dry, white, glairy mucus. The chest was clear. Frequent squeaks were heard over the trachea. The heart rate was 100, the rhythm was regular. The heart was somewhat enlarged to the left. There was a soft systolic murmur at the apex. The blood pressure was 186 systolic, 98 diastolic. The abdomen was obese and soft, with diffuse tenderness in the epigastrium. Pelvic examination was negative. There was no edema. The reflexes were equal and normally active.

The temperature was 103°F. rectally, the pulse 115, and the respirations 40.

Examination of the urine showed a specific gravity of 1.028 and was negative except for the presence of 5 white cells per high-power field. A urine culture showed no growth. The blood showed a red-cell count of 4,560,000 with 64 per cent hemoglobin, a white-cell count of 25,900 with 89 per cent polymorphonuclears, no abnormal cells in the blood smear. Agglutination tests for typhoid, paratyphoid and undulant fever were negative. A van den Bergh was normal, indirect. Two blood cultures showed no growth. A throat culture showed a moderate growth of beta-hemolytic streptococcus. A lumbar puncture showed an initial pressure of 180 mm. There were no cells. The total protein was 17 mg. per 100 cc., sugar 169 mg., and the goldsol curve 0100000000. A spinal-fluid Wassermann test was weakly positive. An electrocardiogram showed a rate of 110 with normal rhythm. The P-R interval was 0.18 second, QRS duration 0.12 second. T_3 was inverted, QRS 1, 2, 3 and 4 notched.

On the third hospital day physical examination was essentially unchanged. There were questionable rales at both bases, but examination was difficult because of a large obese chest wall. There was no stiff neck. Reflexes were hypoactive. Neurological examination was otherwise negative.

On the following day she was mentally dull and still acutely ill. She complained of joint pain and pain across her upper abdomen. There was limitation of motion of the right wrist with pain, and some pain on moving the right elbow. The abdomen was greatly distended in the upper half and rigid over the left upper quadrant. Palpation in the upper abdomen apparently caused pain. No peristalsis was audible in this region. A surgical consultant found that the upper abdomen was extremely tender especially in the left upper quadrant. Spasm could not be determined because of obesity. Peristalsis was normal. She had not vomited. Examination of the urine at this time revealed a trace of bile. Her white-blood-cell count ranged between 15,000 and 27,000. An x-ray film of the chest revealed no evidence of pulmonary disease. On the following day a gastric aspiration showed 400 cc. of recently ingested fluid which was guaiac negative. The stool was brown, liquid; a guaiac test was negative.

The abdomen was tapped in three different places and nothing was found. On the sixth hospital day rales were heard at both bases. A chest film showed some consolidation in the medial portion of the left lung. Her temperature, pulse and respirations had remained essentially the same since entry. She rapidly failed and died on the eighth hospital day.

Differential Diagnosis

Dr. Alvah H. Gordon:* When I was given the opportunity of speaking here, I said, "Timeo Danaos et dona ferentes," and now I have much sympathy with Daniel when he was introduced into the lion's den. I am not familiar with the rules of this game, but I believe all the pertinent information is on this sheet. If it is, I am afraid I am in trouble.

On reading this story, one is impressed by the first few words, "A fifty-year-old female Negro nurse complaining of fever, generalized aching and sore throat of three weeks' duration." Of course that would immediately suggest an agranulocytosis, but as one looks farther down he realizes that there is nothing in that, because the white-cell count is 25,900 with 89 per cent polymorphonuclears. The next thing we come across is the statement that for fifteen years she had had severe pains, in the right upper quadrant of the abdomen, of sudden onset and occurring frequently. The obvious inference is that an obese woman has suffered from attacks of cholelithiasis, which is a reasonable supposition. Then having taken that for granted, if we may do so for a few moments, we pass on and go through the story and find the development of sore throat from an acute infection with the *Streptococcus hemolyticus* which any of us might develop whether we had acute cholecystitis or not. Then later on she developed a pain in the upper abdomen of a quite acute type, and in one instance it is stated that there was some spasm in the left upper quadrant. The acute pain in the upper abdomen and the tender areas both suggest the possibility of pancreatitis which had developed on the basis of previous cholecystitis. There are two or three things which are against that, however. There is one which directly suggests it. The cerebrospinal fluid sugar was 169 mg. per 100 cc. which would indicate that possibly the blood sugar may also have been elevated even though there was no sugar in the urine. We have no figures for the blood sugar so we have to infer without having actual knowledge. However, there are two strong points against the diagnosis of acute pancreatitis. One is that there was no vomiting, and so far as my own experience goes, acute pancreatitis without vomiting must be a very rare occurrence. Another interesting point is that a surgeon saw her and apparently nothing was done. That is considered significant. So, while it is all very true that an acute pancreatitis might very reasonably give rise to her abdominal symptoms, there are some things which it does not account for. It does not account for the fact that she had pain over the upper portion of the chest, and while her temperature and pulse were of moderate range her respirations were definitely elevated beyond the rate which would be suggested by the elevation of the temperature and pulse. Just here one must interrupt oneself and speak again of the disease which when it is diagnosed is rarely present, and when present is rarely diagnosed, that is periarteritis nodosa. There is no doubt that this story throughout might quite readily be present with periarteritis nodosa. One of the very few cases which I have seen came on with an extreme sore throat, such as this patient had, and at the same time with many signs in the chest indicating the presence of pneumonia, and without any suspicion of the disease (periarteritis nodosa) until it was found postmortem.

To come back to the thing that offers the most likely explanation: there is scattered from place to place throughout the story, evidence that this woman had had acute rheumatism, and at various times, pains here and there in certain joints. They are specifically stated as being present in joints. She had fever. Then she developed a sore throat, with the finding of a hemolytic streptococcus. That, too, is a pretty common occurrence in the presence of rheumatic fever or rheumatic infec-

*Professor of medicine, McGill University, Montreal, Canada; physician, Montreal General Hospital.

tion. More than that, with the onset of acute infection, the acute manifestations of rheumatic disease may appear. Among these is acute pericarditis. We find the statement that her heart was somewhat enlarged to the left, to say nothing about the right. No mention is made as to whether she had or had not a pericardial friction. I think it would be unwise to mention that even if it were present.

Dr. Tracy B. Mallory: We would not hold anything like that back. Everything is here, sir.

Dr. Gordon: But I am still more like Daniel in the lion's den. To me, looking at it from that standpoint of the most likely explanation of the story, the upper abdominal pain is quite compatible with acute pericarditis, as are also the pain across the front of the chest and the rapid respirations, and the background of rheumatic infection and infection of the throat, and the development of the terminal symptoms which she showed. There is one point that is difficult to explain under the present circumstances, that is the high cerebrospinal fluid sugar. There is no evidence that she had any of the intracranial causes for such elevation.

Perhaps I might see the x-ray films of the chest.

Dr. A. Thornton Scott: Is that correct about the cerebrospinal sugar? I do not remember anything about its being elevated.

Dr. Mallory: It is down as that in the record.

Dr. George W. Holmes: Unfortunately these are portable films and do not give so much information as they should. She has a very high diaphragm with obesity. The lungs are less clear than I would expect them to be in an ordinary film. The films were taken with the patient lying on her back at a rather close distance and the apparent, wide heart shadow is not so reliable a finding as in films taken the regular way. The first films were taken on the twenty-eighth, and this one on the thirty-first, three days later. The last film is so distorted that we will have to discard it as being of very little value. I do not see anything in the lung field that I would interpret as being abnormal. The heart shadow is certainly somewhat increased in size in these films, but we have to take into consideration the things that I have already mentioned and discount that considerably. However, I think it would be fair to say there is enlargement of the heart shadow. The various chambers of the heart can be made out and there is only moderate increase in the supracardiac shadow. That would be against an accumulation of fluid in the pericardium. A small amount, 300 cc., might be present in such a case without showing any more distortion of the heart shadow than this does. Certainly there is no large amount of fluid and no evidence of fluid in the pleural spaces.

Dr. Gordon: My final conclusion is that the probability in this case lies with acute hemolytic streptococcal infection and the development of rheumatic plastic pericarditis. My own belief is that there was also a small amount of fluid present in the pericardial sac. The other suggestions that I have mentioned in the beginning I believe were probably not correct (agranulocytosis, periarteritis nodosa, acute pancreatitis).

Dr. John H. Talbott: I admire Dr. Gordon's discussion. Each morning on the visit we would go over the list of diagnostic possibilities and discard them one by one. The last note on the record is the one that best expressed our sentiments. This stated that we had no idea what the patient died of.

Clinical Diagnoses

Pancreatitis?
Perforated peptic ulcer?
Bronchopneumonia.

Dr. Gordon's Diagnosis

Acute rheumatic pericarditis.

Anatomical Diagnoses

Acute rheumatic pericarditis.
Rheumatic myocarditis.
Chronic cholecystitis and cholelithiasis.
Pulmonary congestion and edema.
Obesity.
Cortical adenoma of the adrenal.

Pathological Discussion

Dr. Mallory: The only clinical diagnosis we found listed on the autopsy permission sheet was obesity. At postmortem examination the peritoneal cavity was absolutely negative except for a few areas of petechial hemorrhage low in the pelvis which I think were probably on a circulatory basis and insignificant. The pericardium, in contrast, contained about 175 cc. of turbid fluid, conclusive evidence of acute pericarditis. The heart was considerably hypertrophied, weighing about 420 gm. All the valves were absolutely negative. The coronaries showed minimal atheroma with no significant narrowing. The myocardium was a little abnormal in gross appearance, enough so that a frozen section was done at the time of autopsy. That has since been confirmed with many other sections and I have seen only one other heart that contained as many Aschoff's nodules as this one. That other instance, incidentally, also occurred in an individual

over fifty years of age but one who had had little or no previous evidence of acute rheumatic fever. There were a few stones in the gall bladder which I think account satisfactorily for the repeated episodes of pain in the right upper quadrant. A cortical adenoma of the adrenal about a centimeter in diameter was also found but apparently played no role in the symptomatology.

CASE 25232

Presentation of Case

A seventy-three-year-old white woman was admitted complaining of pains across the upper abdomen of two weeks' duration.

For the past six months she had not been entirely well but had no definite symptoms. Three and a half weeks before admission she was thrown forward in a street car, suffered a twist and was somewhat dazed. She remained in bed for the next week. Two weeks before entry she noted the onset of upper abdominal pain located along an arc the center of which lay about 5 cm. above the umbilicus, the ends lying 10 cm. to each side of the umbilicus. The pains radiated from left to right and caused nausea and vomiting. She vomited practically everything she ate during the last two weeks. The pain did not awaken her at night and did not cause her to cry out but at times did cause her to double up. With the onset of the pain two weeks before entry she noted the appearance of a yellow tint to her skin. Both her urine and stools became very dark. She had not had numbness or tingling of the extremities. During the last six months she had lived by herself and had done her own cooking. Her appetite had been increasingly poor for nearly a year. She ate some meat about five times a week but only few vegetables and little fruit. She had lost some weight.

Physical examination showed a well-developed and nourished woman who was slightly but definitely jaundiced. The tongue was atrophic. There were no other definite physical findings. Pelvic and rectal examinations were negative. The blood pressure was 120 systolic, 70 diastolic.

The temperature was 99.2°F., pulse 70, respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 2,070,000 with 50 per cent hemoglobin and a white-cell count of 11,500 with 75 per cent polymorphonuclears. There was no achromia, but there was moderately marked variation in size of the red cells, some larger than normal. No oval cells were seen. There was considerable polychromatophilia and stippling in the large cells, but no nucleated red cells were seen. The platelets were normal. A reticulocyte count was 14.9 per cent. The hematocrit was 24, cell volume 9.3. The icteric index was 25. A blood Hinton test was negative. Stools were of normal color and the guaiac test was negative.

X-ray films of the chest showed the right diaphragm to be unusually high in position. It was smooth in outline and suggested enlargement of the liver. There was an irregular density occupying the right cardiophrenic angle and there was also hazy density along the lung markings extending to the left base. The upper lung fields were clear. The heart shadow was a little prominent in the region of the left ventricle. The aorta was tortuous and there was calcification in the arch. A lateral view of the skull showed irregular thickening of the frontal bone due to frontal hyperostosis. A gastrointestinal series showed a normal gastrointestinal tract except for a small hiatus hernia. The Graham test was negative.

On the third hospital day the liver was found to be palpable 3 cm. below the right costal margin. The spleen was definitely palpable. Liver extract was given intramuscularly on the third, fourth, fifth, eighth, tenth, eleventh, twelfth and thirteenth days. On the fourth, fifth, sixth, seventh and eighth hospital days the reticulocyte counts were 11.5 per cent, 11 per cent, 13.9 per cent, 13.6 per cent and 14.2 per cent respectively. On the ninth hospital day the red-cell count was 2,590,000, hemoglobin (photometric) 8.0 gm., white-cell count 7600. No nucleated red cells were seen. A fragility test showed hemolysis beginning at 0.42 per cent saline and was not complete at 0.24 per cent saline. A control showed hemolysis beginning at 0.42 per cent, complete at 0.28 per cent. Tests for urobilin and urobilinogen in the urine were positive and the foam test bile was positive. Stool examinations continued to show normal color and a negative guaiac test. On the thirteenth hospital day the reticulocyte count was 15.4 per cent and four days later 22.7 per cent. The patient slept most of the time. Edema of the feet had developed. On the fifteenth and sixteenth hospital days she was disoriented. There was definitely less motion in the left cheek and mouth. Rales appeared at both lung bases. On the eighteenth hospital day her pulse became weaker. Asthenia increased. Shortly after midnight she became cold, dyspneic, had air hunger, became comatose and died.

Differential Diagnosis

Dr. F. T. Hunter: I should like to make some comments on this history. To begin with, her appetite had been poor for nearly a year; she had

not been entirely well and for six months she had been doing her own cooking. We cannot judge about the cooking. It possibly was so poor that her appetite decreased, yet I think there is more behind her lack of appetite than her gastronomic endeavors in the kitchen.

We are not informed whether the ankle, the abdomen or the neck was injured. We shall have to leave that question aside for the moment. She was dazed. I think most people are when a car stops suddenly, or when they get hit,—particularly women.

She stayed in bed the next week. I am interested to know why. Was it because of the shock or pain, although the pain was not supposed to have come on until later? Did her doctor advise her to stay in bed, or did her lawyer? If it was her lawyer I presume we can neglect this whole accident as a cause of her subsequent illness.

Nothing is said about the character of the pain. We are told it was definitely localized in the upper abdomen and did not wake her at night. I should imagine it was colicky pain. It certainly was related somewhat to position, because when she was lying in bed at night it was better, or at least it did not bother her. Vomiting, however, continued. I should like to know whether she had medication. Did her doctor give her morphine? Old people will sometimes vomit after morphine or at least have nausea. At about this time it was noticed that she had a yellow tint to the skin. We would like to know whether it had been present before, or whether her doctor called her attention to it, that is, if she had a doctor.

The dark stools are apparently not due to blood because later on the guaiac test was negative. When in the hospital pernicious anemia was suspected because mention is definitely made that she had no numbness or tingling.

She probably had an inadequate diet. She had lost weight, but we do not know how much. Ordinarily, people are vague about loss of weight; if they lose twenty pounds or more they notice it, but "some" weight loss usually means five or six, possibly ten pounds. Her loss of weight may be due to the fact that she had not eaten much for a couple of weeks.

Physical examination states that she was well developed and nourished. If she had carcinoma in the abdomen involving the liver or bile ducts I do not believe that she would have shown good nourishment at the time of examination. Furthermore, I think she probably would have had a longer story of pain. The jaundice was definite. The tongue was atrophic. We have no knowledge as to whether or not it had ever been sore—presumably not. So in the physical examination we find a well-nourished woman with jaundice and an atrophic tongue and we think right away of pernicious anemia. The slight increase in temperature would go perfectly well with that diagnosis, but the temperature could also go with carcinomatosis.

"Examination of the urine was negative." If this is correct she certainly did not have obstructive jaundice because if you can see jaundice in the skin you are certainly going to have bile in the urine even by the crude test of shaking a test tube of urine.

So far we are thinking of pernicious anemia. The first thing that seems odd is that the white count is high and the polymorphonuclear count unusually high for this disease. There is no mention as to whether myelocytes were seen in the blood smear or whether the polymorphonuclears showed multiple lobulation such as you see in pernicious anemia. The variation in size of the red cells goes with any type of anemia of this severity. The next point of interest is that there were no nucleated red cells found. They were thinking of cancer metastases in the bone marrow. The reticulocytes were 15 per cent. The first thing that comes to mind is hemolytic jaundice. I have seen a blood smear of a child with this disease with 87 per cent reticulocytes. The cell volume was higher than normal. If the cell volume is based on the recorded two million count, according to my figures it should be 11.6; but I presume there was another count done on the venous blood which brought that figure down to 9.3. It would be helpful to know whether the van den Bergh was diphasic or indirect. The stool was normal in color, with no blood. We would like to know whether she had been given any liver extract either by mouth or by injection by the doctor who took care of her before she came in, that is if she had a doctor. The icteric index of 25 is high I should think for pernicious anemia with a red count of two million.

We have no definite information in regard to the date of this x-ray film of the chest, whether it was made just before death, or on entry to the hospital. I should like to know why the skull plate was taken. Were they looking for metastases, Paget's disease, or were they still looking for something resulting from the streetcar ride? If the gastrointestinal series is normal I should like to be sure that there is no displacement of the duodenum by tumor in the region of the pancreas. The Graham test was negative, and therefore I think the van den Bergh test would have been indirect if it had been done, because with a diphasic van den Bergh, the Graham test is

usually positive, that is, the gall bladder fails to fill, or fills only faintly. May we see the x-ray films?

Dr. George W. Holmes: The record states that the diaphragm was high on the right. I think it is, but I would not be at all certain that it was due to a large liver. It may be. In the other films where the liver is particularly well seen it does not seem to be enlarged. I do not see the spleen. She has something in her lung in the angle between the diaphragm and the heart which could be a destructive process or collapse. That may account for the high position of the diaphragm. These films were probably taken at full inspiration and anything that would cause her to fix her diaphragm on that side would also account for the high position. I think the films actually offer less information than one would assume from reading the record. The gall bladder is rather faint but is about normal in size and contracts after food, and I think we have to interpret it as negative. This film of the skull shows exostoses in the frontal region which so far as I know are of no importance.

Dr. Hunter: What about the date of the chest film?

Dr. Tracy B. Mallory: The chest plate was taken on the tenth day.

Dr. Hunter: She died on the eighteenth. It seems that we derive no further information from the x-ray examinations. The important information we do obtain about this patient comes from her course in the hospital. The liver was palpable 3 cm. below the costal margin. I assume that was found after the x-ray report was turned in. The spleen was said to be palpable on the third day and that corresponds to the time when the visiting man probably felt it. Liver extract was given. The first question we want to bring up is whether or not she was given potent material, because if a potent extract is given we do not usually see pernicious anemia developing a reticulocyte count so high as this and having it remain constant. On the ninth hospital day the red-cell count had apparently increased by a half a million; the white-cell count had fallen somewhat, and they kept looking for nucleated red cells.

Dr. Mallory: A potent extract was given from the start.

Dr. Hunter: In pernicious anemia the spleen is enlarged and palpable in a small percentage of cases, perhaps 15 or 20 per cent. Nowadays we are apt to find very few enlarged spleens because patients are diagnosed and treated before they have the anemia long. The fact that there were no nucleated red cells is against this being metastatic tumor in the bone marrow. In relation to a diagnosis of hemolytic jaundice, the fragility was normal. Moreover, I should be amazed to find a woman of seventy-three with congenital jaundice manifesting itself for the first time at her age. I do not believe the foam test on the urine was positive, because urates often give a yellowish red color to the foam.

Suddenly, on the seventeenth day, the reticulocytes jumped to 22.7 per cent. We want to know whether this was a delayed response, or a terminal attempt of a pernicious anemia marrow to turn out red cells. In regard to the tendency to sleep we should have to inquire into the medication given. The edema of the feet was probably mild cardiac failure plus anemia in a woman of seventy-three.

She became drowsy, and there was definite evidence of something happening in the right cerebral hemisphere because of the evidence of paralysis on the left side of the face. The rales heard could have been due to cardiac decompensation, or to a hypostatic pneumonia. The rest of the story tells nothing except that she finally died.

When we go back over this whole story there are several things that make us consider this a case of pernicious anemia which has failed to respond to treatment. The possibility of hemolytic jaundice I am going to discount right away because of her age and the lack of other evidence. I am going to say definitely that I do not think the streetcar accident had anything to do with her death because she had a normal abdomen; and I do not believe that had there been an injury to a viscus she would have had a perfectly normal abdomen. To account for the pain, she might perfectly well have injured her spine; otherwise I cannot account for it.

I am going to make a diagnosis of pernicious anemia which failed to respond, and, possibly, cerebral thrombosis. She probably had a terminal pneumonia and, perhaps, mild congestive failure. Whether or not a spinal injury will be found, I do not know. Those are the diagnoses that I have to stand by, but I feel like the musician playing a Debussy quartette, who said after he got through that he knew every note was wrong, but he did not dare change it because he might be right.

Dr. Milton H. Clifford: The story this woman gave when she came in was just as troublesome as Dr. Hunter has found it. I believe it was her lawyer who told her to go to bed for the first week. She had had very little medical attention. Her family had known that she was not in good health but nothing came to a head until this accident, the details of which could not be obtained any more satisfactorily than has been recorded here. She was fairly well nourished. She had had no liver therapy before entry so far as

we know. On entry probably the reason the liver was not felt is that she held herself quite rigid and had some distention at the time. The results of abdominal examination varied, although the liver could be felt and a mass in the left upper quadrant could be made out which I presumed to be spleen. She continued to be drowsy the whole of her course and did not respond to liver therapy.

Dr. Wyman Richardson: I think it is fair for me to say that I was more impressed by the upper abdomen than the examiner who is quoted in the record and I was not so certain that it was spleen we felt. The other thing I should like to say is that I am much interested in the picture like this that simulates hemolytic anemia. I have seen it in another case of the same type and the remembrance of that case led me to make a fairly good guess in regard to this one. I think it probably will not be a hemolytic anemia, but there may be another cause for the jaundice and the reaction of the bone marrow may be the reaction to this disease that Dr. Mallory is going to tell us about.

Dr. Mallory: You did not think that the spleen was palpable?

Dr. Richardson: I did not, but Dr. Clifford thought that it was.

Dr. Hunter: Where am I left then?

Clinical Diagnosis

Carcinomatosis.

Dr. Hunter's Diagnoses

Pernicious anemia.
Bronchopneumonia (terminal).
Cerebral thrombosis?
Congestive failure (mild)?

Anatomical Diagnoses

Carcinoma of the pancreas with metastases to the liver.
Pernicious anemia.
Bacterial endocarditis, acute terminal, mitral and aortic.
Jaundice, slight.

Pathological Discussion

Dr. Mallory: The autopsy on this patient showed a carcinoma of the body and tail of the pancreas which had grown around the splenic artery and vein and practically occluded them. The spleen weighed only 100 grams so I feel quite sure it was not felt and the mass must have been pancreas. The liver was two-thirds or three-fourths replaced by carcinoma although it was only moderately enlarged. We rather thought at the end of the autopsy that we had satisfactorily explained the case and we assumed that the anemia without much question was due to widespread metastases to the bone marrow and could be classed as myelophthisic anemia. When the sections came through we found that this was not the case. There were numerous sections of bone marrow without the slightest evidence of metastases and the bone marrow was entirely consistent with pernicious anemia. It shows a marked red-cell hyperplasia with considerable numbers of megaloblasts. Ordinary types of anemia almost never show megaloblasts in significant numbers, and in this hospital in adults we have seen such large numbers of megaloblasts only in pernicious anemia and two cases of benzol poisoning. So I am inclined to believe that she did have pernicious anemia. Possibly she had the very similar macrocytic anemia that is occasionally seen in liver insufficiency. I cannot rule that out. She had one other complication which I think unquestionably had a good deal to do with the exitus, that was a terminal bacterial endocarditis. She had no examination of the head, but I imagine that was embolism from bacterial endocarditis.

Dr. Holmes: Was there any gross change in the shape of the liver?

Dr. Mallory: No.

Dr. Holmes: Anything in the lungs?

Dr. Mallory: There was atelectasis in the right lower lobe and also several small metastatic nodules.

Dr. Bernard M. Jacobson: There are in the literature several cases of pernicious anemia with diffuse pancreatic disease, usually chronic pancreatitis with fibrosis.

Dr. Mallory: In this case the head of the pancreas was quite normal, but the body and tail were entirely replaced by carcinoma.

Dr. Richardson: I wonder if it is fair to call this pernicious anemia on the basis of the finding of a few megaloblasts in the bone marrow. I have an idea that what we often refer to as a myelophthisic anemia is not in fact due to actual crowding of the bone marrow by tumor cells. We have seen patients with widespread malignant disease who showed a leukemoid picture and it is, of course, common to get an anemia with much evidence of marrow activity as shown by the presence of nucleated red blood cells in all stages of maturity. In this case I wonder whether there may not have been malignant disease in some parts of the marrow not examined pathologically which brought about such a regenerative blood picture, and if the jaundice in this case might not have been due to the extensive malignant involvement of the liver. Such a picture superficially resembles a hemolytic anemia.

DR. MALLORY: I must confess to almost complete ignorance of the bone-marrow picture in patients with macrocytic anemia dependent on hepatic insufficiency. I have made no personal study of it and I have seen few reports in the literature. Wintrobe and Shumacker* mention the bone marrow in two cases which came to autopsy: in one it was reported merely as moderately hyperplastic, in the other as normal. I have, therefore, assumed it would not be readily confusable with that of pernicious anemia, but my evidence is scant.

As regards myelophthisic anemia we have felt that the major part of the bone marrow must be diffusely replaced by tumor before it develops and therefore one could hardly miss it at autopsy if three or more flat bones were sampled. Moreover, such cases when the anemia is severe almost always show extramedullary hematopoiesis in the liver and the spleen as a further check upon one's diagnosis. In fact we have raised the hypothesis that this extramedullary red cell formation might well be responsible for one of the most important clinical indications of myelophthisic anemia in the presence of nucleated red cells in the blood smear even without profound anemia. It is easy to imagine that nucleated cells could slip more easily out of the sinusoids of soft and mobile organs like the liver and the spleen than from sinuses of the bone marrow with their bony encasement.

*Wintrobe, M. M., and Shumacker, H. S. Jr.: The occurrence of macrocytic anemia in association with disorder of the liver, together with consideration of relation of this anemia to pernicious anemia. Bull. Johns Hopkins Hosp. **52**:387-407, 1933.

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SEVENTIETH ANNIVERSARY OF THE CHILDREN'S HOSPITAL

On June 8, 9, and 10, the Children's Hospital is celebrating the seventieth anniversary of its founding and the fiftieth anniversary of its nurses' training school. Graduates of the hospital have returned from all parts of the United States. The scientific program, which may be found in detail on another page of this issue of the *Journal,* is being presented by representative graduates of the departments of medicine, surgery, orthopedic surgery and pathology. A scientific exhibit by the present members of the hospital staff is now on view at the hospital.

The Children's Hospital was founded in 1869 by a group headed by Dr. Francis Henry Brown, who had determined "to supply a want in our community which has been felt in our medical schools; namely, an opportunity to study infantile diseases. These, as every mother and every nurse knows, are so sudden, so fluctuant, and so mysterious, and often so rapid in their fatality, that they furnish a distinct branch of medical science, the importance of which can hardly be overestimated." The first home of the hospital was a small house on Rutland Street equipped for the care and study of twenty patients. Shortage of space forced the hospital to transfer its quarters to a rented house on Washington Street the following year. In 1882 the Huntington Avenue building of the Children's Hospital was built, and in its first year two hundred and eighty ward patients were cared for, and one thousand four hundred and eighty-eight outpatients. Steadily increasing demands forced the transfer of the hospital in 1914 to its present location adjacent to the Harvard Medical School. The new hospital was finally brought into its present form between 1929 and 1931 with the addition of new quarters for neurology, contagious disease and pathology, and improved quarters for patients suffering from surgical diseases of infancy. This last building program permitted the hospital to realize its greatest ambition of being in every sense of the word a *general hospital for children.* Last year the hospital cared for approximately seventy thousand children, over five thousand of these on its wards; the budget exceeded half a million dollars. With beds for two hundred and eighty-three ward patients, a private ward, a staff of about one hundred and fifty doctors, well-equipped laboratories for routine and research work, a nurses' training school, facilities for the teaching of students and the training of young doctors, and a close affiliation with its sister institution, the Infants' Hospital, the hospital today is successfully carrying out the original aims so wisely set forth by the managers in 1869:

> The medical and surgical treatment of the diseases of children.
>
> The attainment and diffusion of knowledge regarding the diseases incident to childhood.
>
> The training of young women in the duties of nurses.

The nurses' training school is widely known. Its graduates hold many teaching and administrative

positions. Most of the teaching of pediatrics at the Harvard Medical School is carried on at the Children's Hospital. The interns and resident physicians of the hospital have come from and gone to all parts of this country and many foreign countries. The contributions of the staff of the hospital to medical literature are read throughout the world.

Thus the Children's Hospital not only provides good medical care for the sick of today but also contributes to the provision of better medical care for the sick of tomorrow.

ACTA MEDICA URSS

PHYSICIANS and medical libraries in the United States will welcome the new international journal of medicine, founded by the young commissar of public health, Nicolai Ivanovitch Propper-Grachtchenkoff,* entitled *Acta medica URSS*. The first two numbers have already appeared, and the papers form a noteworthy collection dealing with many spheres of medical thought and embracing both experimental and clinical medicine.

The new public-health commissar was head of the department of sensory physiology in the All-Union Institute of Experimental Medicine at Moscow before he assumed the heavy duties of directing the public health of the Soviet Union. Dr. Propper is well known in this country since his sojourn as fellow of the Institute of Experimental Medicine, Moscow, in 1936-37, when he carried out studies at the Rockefeller Institute for Medical Research in New York City and at the Laboratory of Physiology at Yale University. The first paper of the first number of *Acta medica URSS* is by Dr. Propper and deals with the role of medical science in the practice of public health; the paper displays a wide knowledge of world medicine, which is rare among Soviet writers. He states that one of the objects of this new journal is to make physicians of the Soviet Union cognizant of progress in world medicine and that he hopes it will also promote a free interchange of ideas between the physicians of Russia and those in other countries of the world. There is no trace of chauvinism in Dr. Propper's writing and one trusts that the new journal which he and Dr. M. Serejski, the editor, have launched will have the enthusiastic reception which it so richly deserves both in their own country and abroad.

In the prefatory note it is stated that the editorial offices will receive papers in four international languages, Russian, French, English and German. The journal accepts original contributions, and it also reprints papers of importance culled from medical journals elsewhere in the world.

It may interest readers of the *Journal* to learn that the new public-health commissar is doing much to arouse interest in the history of medicine in Soviet Russia. He has already issued a Russian translation of Harvey's *De Motu Cordis* (1628), Galvani's *De Viribus et Electricitatis in Motu Musculari* (1791) and Trembley's celebrated monograph on the Hydra (1744). Other important reprints and facsimiles will be issued by the Commissariat of Public Health at Moscow in the near future. Russian editions of our great medical classics give interest and zest to bibliographers and collectors in the field of medical history, and we hope that Dr. Propper may long continue to promote in his own country the finer cultural and scientific traditions of the art.

*In physiological literature the commissar is known as "N. I. Propper," the compound cognomen "Propper-Grachtchenkoff" being used only in Russia. Dr. Propper's more important recent papers are as follows: "Sensitization" by injury of the cutaneous nerve endings in the frog. *J. Physiol.* 88, 388-400, 1937 (with Francis Echlin); Sensory fibres in the spinal accessory nerve. *Ibid.* 92, 160-166, 1938; Nature neuro-humorale de l'épilepsie. *Rev. neurol.* 70, 332-345, 1938; Nature physiologique de la douleur. *Acta med. URSS* 1, 113-135, 1938.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

BLEEDING IN THE PUERPERIUM

Mrs. R. L., a twenty-year-old gravida I, began to flow very freely on November 26, 1938, five days after a normal, full-term delivery.

The family history was negative. The patient had had measles as a child. Her tonsils had been

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

removed, as well as a cervical polyp. Catamenia began at fifteen and were regular with a twenty-eight-day cycle. The last period was February 16, making her due for delivery from November 23 to November 26. Her pregnancy had been uneventful. The delivery was normal and it was felt that the placenta was intact.

Convalescence after delivery was uneventful until November 26 at 10 a. m. when the hospital telephoned that she was flowing a great deal and had passed several large clots. She was given Ergoklonin, but since the flowing did not cease and it was estimated that she had lost about 500 cc. of blood, it seemed wise to explore the uterus. The patient was typed and matched for possible transfusion. Her husband was found to be a compatible donor.

Under gas-oxygen anesthesia and strict asepsis, examination showed the uterus in good anterior position, well contracted and not much larger than a normal uterus five days post partum. The internal os admitted one finger. A definite piece of placenta was found adherent at the fundus and as much of this as possible was removed with the finger, dull curet and ovum forceps. An iodine pack was left in the uterus and was removed forty-eight hours later. After removal of the pack she passed a small clot and a piece of placental tissue. There was no flowing that night, but the next morning, November 29, she passed another clot which was mostly tissue. On December 1 she passed still another piece of tissue to which a good-sized clot adhered. Her pulse was under 70 and since her blood pressure had, at no time, gone below 110-120 systolic she was left alone. There was no bleeding after the expulsion of the clot on December 1, and she was discharged on December 11.

There was no abnormal flowing at the time of her first period after the birth of the baby.

DATE	RED-BLOOD-CELL COUNT	HEMOGLOBIN
1938		%
Nov. 22	4,600,000	90
26	4,400,000	86
27	4,200,000	82
28	4,200,000	80
29	3,700,000	75
30	3,000,000	65
Dec. 1	3,250,000	65
2	3,100,000	62
3	3,320,000	68
4	3,420,000	74
6	3,250,000	73
8	3,800,000	75
10	3,900,000	82

The pathological report of the pieces of placenta obtained at the time of operation was as follows: "Decidua-like cells, extensive necrosis and chronic inflammation, a few cells of trophoblastic type, but no definite chorionic villi."

Comment. This is another illustration of the commonest cause of bleeding in the puerperium. At the time of the delivery of the placenta it is clearly remembered that the placenta seemed intact. There was a great deal of blood lost at the time of the initial hemorrhage, and it is surprising that the blood picture does not bear this out. It is of course possible that the blood figures are incorrect. The convalescence after the removal of the piece of placenta was afebrile, but the blood examinations showed that there was considerable bleeding for several days after the pack had been removed. A second invasion of the uterus was contemplated, but the patient's general condition led one to conservatism. No transfusion was done because the blood examination ruled out its necessity.

It is often observed that the first catamenia after delivery may be very free. This is true more frequently in patients who are not nursing. One may expect a very free period in one who has bled as this patient did, but, fortunately, her first period was normal in every respect.

The strictest asepsis must be observed in all cases requiring intrauterine treatment. One cannot emphasize this too much and must also appreciate that, if a curet is used, it must be used with extreme care and never in a rough manner.

DEATHS

McKEOUGH — WILFRED A. McKEOUGH, M.D., of Haydenville, died May 26. He was in his forty-eighth year.

Born in Nova Scotia, he received his degree from the Tufts College Medical School in 1924. He was assistant to Dr. Francis E. O'Brien, superintendent of the Hampshire County Sanatorium, at the time of his death and had formerly been assistant medical officer at the State Sanatorium, Glencliff, New Hampshire.

Dr. McKeough was a member of the Massachusetts Medical Society and the American Medical Association.

Three sisters survive him.

PARTRIDGE — CHARLES C. PARTRIDGE, M.D., of Melrose, died May 29. He was in his eighty-first year.

Dr. Partridge was a former member of the staff of the Boston City Hospital and practiced for many years in Hyde Park.

He was a former member of the Massachusetts Medical Society.

His daughter, and three sons survive him.

THORNDIKE — PAUL THORNDIKE, M.D., of West Roxbury, died May 28. He was in his seventy-seventh year.

Born in Beverly, he attended the public schools in Milwaukee, Wisconsin, and graduated from Harvard College in 1884. He received his degree from the Harvard Medical School in 1888, and became a member of the staff of the Boston City Hospital the same year. He continued his studies in Vienna and upon his return joined the Harvard faculty as assistant professor of genitourinary surgery. He later became surgeon-in-chief at the Boston

City Hospital and was on the staffs of the Charlesgate Hospital, the Phillips House and many other Boston hospitals. At the time of his death Dr. Thorndike was clinical professor of genitourinary surgery, emeritus, at Harvard Medical School.

Dr. Thorndike was a member of the Massachusetts Medical Society, the American Medical Association, the American Association of Genito-Urinary Surgeons, and the Boston Surgical Club.

A son, Dr. William T. S. Thorndike, and two daughters survive him.

TIBBETTS — Guy D. Tibbetts, M.D., of Antrim, New Hampshire, died June 2. He was in his fifty-second year.

Born in Gloucester he attended schools there and received his degree from Tufts College Medical School in 1911. He served his internship at the Boston City, the Boston State and the Cambridge City hospitals, and then started private practice in Bennington, New Hampshire. Dr. Tibbetts was one of one thousand American doctors loaned to the British Government during the World War, and was awarded the Distinguished Service Cross by King George V.

He was a former member of the Massachusetts Medical Society, resigning in 1921 to join the New Hampshire Medical Society, and was also a fellow of the American Medical Association.

His widow survives him.

MISCELLANY

MANHATTAN CONVALESCENT SERUM LABORATORY

The New York Department of Health announces that that Manhattan Convalescent Serum Laboratory, a nonprofit organization, is prepared to supply measles convalescent serum to hospitals and physicians at the cost of production. The serum is furnished at the rate of 50 cents per cubic centimeter, or $2.50 for 5 cc.

Serum can be obtained at the Manhattan Convalescent Serum Laboratory, Room 610, in the William Hallock Park Laboratory of the New York City Department of Health, 15th Street and East River, between the hours of 9 a. m. and 5 p. m. on all weekdays except Saturday, when the laboratory is open from 9 a. m. to 12 noon. At all other times serum can be obtained from Dr. William L. Wheeler, Jr., 348 West 22nd Street (Chelsea 3-4149).

Further information regarding convalescent serum supplied by the laboratory can be obtained from Dr. William Thalhimer, director.

NOTES

The following promotions on the faculty and teaching staff of Harvard Medical School, effective next September, were recently announced:

Oliver Cope, Francis C. Newton, Stanley J. G. Nowak, and Robert Zollinger, assistant professors of surgery; Otto A. Bessey, associate in biological chemistry; Laurence B. Ellis and Maurice B. Strauss, associates in medicine; George M. Hass, associate in pathology; John A. V. Davies, Lewis W. Hill and Clement A. Smith, associates in pediatrics; Henry K. Beecher, associate in anesthesia; Robert E. Gross, John D. Stewart and Carl W. Walter, associates in surgery, and Henry D. Chadwick, lecturer on medicine.

REPORTS OF MEETINGS

HOSPITAL DAY AT THE BEVERLY HOSPITAL

The annual observation of Hospital Day was held at the Beverly Hospital on Saturday, May 13, in accordance with the custom of having the celebration on the nearest Saturday to National Hospital Day. On this day the former interns are invited to return and spend the day as guests of the staff of the hospital.

The program as presented by the staff was initiated with a surgical clinic, the first case being a partial gastric resection, and the second an exploratory laparotomy for carcinoma of the gall bladder. The operations were performed by Drs. Peer P. Johnson and Richard E. Alt. The following papers were then presented: "Highlights in the Development of Modern Chemotherapy with Special Reference to Sulfapyridine," Dr. Barnard Todd; "Technic of Nailing a Fractured Hip (Beverly Hospital Method)," a motion picture, Drs. Johnson and Alt; presentation of cases by the house staff (Drs. DeWolfe, Epstein, Commette and Todd) with discussions by Drs. A. E. Parkhurst, Johnson, Paul E. Tivnan and C. F. Branch.

NEW ENGLAND SOCIETY OF PSYCHIATRY

The New England Society of Psychiatry held its sixty-fourth annual meeting at the Metropolitan State Hospital, Waltham, April 25, as the guests of Superintendent Roy D. Halloran. The meeting was attended by one hundred and sixty-nine members and guests.

Following inspection of the hospital and an excellent luncheon, the meeting was called to order by President Harlan L. Paine. A few words of welcome by Superintendent Halloran opened the meeting. The minutes of the previous meeting were read and adopted. The report of the treasurer and auditors was submitted and adopted as presented. The following were elected to full membership: Dr. Paul R. Felt, Middletown, Connecticut; Dr. Valerie R. Jurecsek, Howard, Rhode Island; Dr. Adrian Scolten, Portland, Maine; Dr. George L. Wadsworth, Middletown, Connecticut.

The Examining Committee for the best papers published during the calendar year of 1938 recommended that the awards be given to the writers of the three following papers: "The Effect of Adrenalin and Mecholyl in States of Anxiety in Psychoneurotic Patients" by Erich Lindemann and Jacob E. Finesinger; "Pick's Disease: A specific type of dementia" by Ira C. Nichols and Walter C. Weigner; "Studies in Convulsant Therapy. 1. Technique and Clinical Phenomena. 2. The Role of Alkalinization" by Stanley Rochelle Dean.

The following were elected to office: president, Dr. Charles H. Dolloff, Concord, New Hampshire; vice-president, Dr. Roy D. Halloran, Waltham, Massachusetts; secretary-treasurer, Dr. George A. Elliott, Middletown, Connecticut; councilors, Dr. George E. McPherson, Belchertown, Massachusetts, and Dr. Harlan L. Paine, North Grafton, Massachusetts.

The meeting adjourned following the reading of the paper, "Some Observations on Patients Diagnosed as Having Schizophrenia," by Dr. John W. Thompson, of the Harvard Fatigue Laboratory and the research staff of the Metropolitan State Hospital, and Dr. William Corwin, of the Metropolitan State Hospital.

NOTICES

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra cordially invites the medical profession to tune in on Station WEEI Sunday evening, June 11, at 8 o'clock to hear its first family concert.

SEVENTIETH ANNIVERSARY OF THE CHILDREN'S HOSPITAL

The seventieth anniversary celebration of the Children's Hospital will be held in Vanderbilt Hall, Friday and Saturday, June 9 and 10.

* * *

MEDICAL PROGRAM

Friday, June 9

8:00 a. m.–9:45 a. m. Selected operations by surgical and orthopedic services.

9:45 a. m. First scientific session: Dr. W. E. Ladd, chief of the Department of Surgery and clinical professor of surgery, Harvard Medical School.

Opening remarks. Dr. Ladd.

Words of welcome. Dr. Paul Emerson, president of the Children's Hospital Alumni Association.

Remarks and announcements. Dr. P. J. Mahoney, secretary of the Children's Hospital Alumni Association.

The Children's Hospital Today. Dr. Sidney Farber, secretary of the visiting staff of the Children's Hospital.

10:15 a. m.–12:30 p. m. Certain Aspects of the Protein Metabolism of Premature Infants. Dr. S. Z. Levine, professor of pediatrics, Cornell University Medical College.

Correlation of the X-ray and Autopsy Findings in Lipoid Pneumonia. Dr. R. S. Bromer, assistant professor of radiology, Graduate School of Medicine, University of Pennsylvania.

Some Studies of Body Water in Normal and Abnormal Growth. Dr. Bengt Hamilton, associate professor of pediatrics, University of Illinois.

Studies on the Blood Level of Co-Enzyme I (Cozymase) in Nicotinic Acid. Dr. S. O. Dexter, Jr., The Rockefeller Institute Hospital.

The Bridle of Theages. Dr. J. A. Nutter, clinical professor of orthopedic surgery, McGill University.

Intra-mesenteric Diverticula. Dr. J. W. Duckett, associate professor of clinical surgery, Baylor University.

Children's Surgery as a Specialty. Dr. H. C. Coe, Seattle, Washington.

Training Crippled Children. Dr. J. F. Pohl. (Talk and moving pictures.)

1:45 p. m.–4:15 p. m. Second scientific session: Chairman Dr. F. R. Ober, chief of Department of Orthopedic Surgery, and professor of orthopedic surgery, Harvard Medical School.

The Calcium Balance in a Case of Legg's Disease. Dr. J. A. Johnston, pediatrician-in-chief, Henry Ford Hospital, Detroit, Michigan.

Hypoproteinemia. Dr. A. A. Weech, associate professor of pediatrics, Columbia University Medical School, the Babies' Hospital.

Membrane Formation at Lipoid-Protoplasmic Interfaces. Dr. G. M. Hass, instructor in pathology, Harvard Medical School.

Human Locomotion: A summary of twelve years of research. Dr. R. P. Schwartz, associate professor of surgery, University of Rochester.

Acute Appendicitis in Childhood. Dr. Henry Hudson, Jr., assistant in surgery, Harvard Medical School.

On the Acid-Soluble Phosphorus Compounds of Red Blood Cells. Dr. G. M. Guest, associate professor of pediatrics, University of Cincinnati, College of Medicine.

Coronary Artery Occlusions. Dr. Monroe Schlesinger, Jr., Associate in pathology, Harvard Medical School, pathologist to the Beth Israel Hospital.

Saturday, June 10

8:00 a. m.–9:45 a. m. Selected operations by surgical and orthopedic services.

9:45 a. m.–12:00 m. Third scientific session: Chairman, Dr. S. Burt Wolbach, chief of the Department of Pathology and Shattuck Professor of Pathology, Harvard Medical School.

Photometry and Vitamin A. Dr. P. C. Jeans, professor of pediatrics, University of Iowa.

New Shelf Operation for Subluxation of the Hip-Joint. Dr. E. W. Ryerson, senior orthopedic surgeon, St. Luke's Hospital, Chicago, and formerly professor of orthopedic surgery, Northwestern University Medical School.

Hydrometrocolpos in Infancy. Drs. J. W. Chamberlain and P. J. Mahoney, Boston University School of Medicine.

Studies in the Physiology of Premature Infants. Dr. J. L. Wilson, associate professor of pediatrics, Wayne University College of Medicine, Detroit, Michigan.

The Care of Prematures. Isabelle Jordan, R.N., assistant superintendent of nurses, the Children's Hospital, Boston. (Moving picture.)

Surgical Management of the Patent Ductus Arteriosus: With summary of four successfully treated cases. Dr. R. E. Gross, instructor in surgery, Harvard Medical School.

Metabolism of Sulfanilamide. Dr. J. S. Harris, associate in pediatrics, Duke University Medical School.

12:00 m.–1:00 p. m. Clinicopathological conference conducted by the chiefs of the four services: pediatrics, surgery, orthopedic surgery and pathology.

1:00 p. m. Closing remarks by Dr. K. D. Blackfan, chief of the Department of Pediatrics and Thomas Morgan Rotch Professor of Pediatrics, Harvard Medical School.

There will also be numerous exhibits from the departments of medicine, surgery, orthopedic surgery, photography, pathology, administration and roentgenology, the Harvard Infantile Paralysis Commission Clinic, and the School of Nursing.

SYMPOSIUM ON CARCINOMA OF THE TONGUE

A symposium on carcinoma of the tongue has been arranged by the staffs of the Massachusetts General, Collis P. Huntington Memorial, Pondville and Palmer Memorial hospitals. A review of cases seen at each of these hospitals will be presented by Drs. Roy E. Mabrey, Ira T. Nathanson, Thomas J. Anglem and Clifford C. Franseen. Discussion will be opened by Dr. Channing C. Simmons.

The meeting will be held on Tuesday, June 13, on the roof of the Palmer Memorial Hospital, at 8:00 p. m. Refreshments will be served.

All members of the medical profession are cordially invited to attend.

LELAND S. MCKITTRICK, M.D., *Chairman.*

LAWRENCE CANCER CLINIC

The regular Lawrence Cancer Clinic, to be held at the Lawrence General Hospital, 1 Garden Street, Lawrence, on Tuesday, June 20, at 10:00 a. m., will be a demonstration and teaching clinic for physicians, with Dr. Channing C. Simmons, of Boston, present as consultant. Physicians of the north half of Essex County are invited to accompany any of their patients whom they desire to have this service or to send them with a note. A report will be returned to every physician who sends a patient. The service is gratis. Any physician is welcome to attend the clinic.

This clinic is endorsed by the Committee on Postgraduate Instruction of the Massachusetts Medical Society.

J. FORREST BURNHAM, M.D., *Chairman.*

GRADUATE FORTNIGHT OF THE NEW YORK ACADEMY OF MEDICINE

The twelfth annual Graduate Fortnight of the New York Academy of Medicine will be held in New York City from October 23 through November 3. The general topic is "The Endocrine Glands and Their Disorders."

As usual the clinical sessions will be held during the day at the various hospitals. During the evening, talks on different aspects of the general topic will be given at the Academy by men who are experts along such lines. The subtopics to be discussed are as follows: "Historical Sketch of the Development of Endocrinology," "Physiology of Anterior Lobe of Pituitary Gland," "Pituitary Hypothalamic Syndromes," "Hypo- and Hyperpituitarism," "Therapeutic Application of Female Sex Hormones," "Physiology and Principal Interrelations of the Thyroid," "Hypothyroidism," "Hyperthyroidism," "Surgical Treatment of Hyperthyroidism and Other Diseases of the Thyroid," "The Adrenal Medulla," "Adrenal Insufficiency," "The Adrenal Cortex," "The Cushing Syndrome: Neoplasms of the adrenal gland," "Overfunction of the Adrenal Cortex," "Relation of Diabetes to the Endocrine System," "The Influence of the Central Nervous System Upon Endocrine Activity," "Physiology and Pathology of Parathyroids," "Hyperparathyroidism," "Physiology of the Ovaries," "Physiology of Testes and Therapeutic Application of Male Sex Hormones," "Puberty, Menstruation and Pregnancy" and "Menopause." A comprehensive exhibit of research, roentgenographic and pathologic material will be assembled to include diagnosis and treatment, clinical and laboratory diagnostic methods, action of drugs and other therapeutic measures. The library will exhibit books relating to the subject.

Registration fee for non-members is five dollars. Further details may be obtained by writing to the New York Academy of Medicine, 2 East 103 Street, New York City.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JUNE 12

MONDAY, JUNE 12

Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Harvard School of Public Health, 55 Shattuck Street, Boston.

TUESDAY, JUNE 13

Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Harvard School of Public Health, 55 Shattuck Street, Boston.

*10 a. m. - 12:30 p. m. Tumor Clinic. Boston Dispensary.

*8 p. m. Symposium on Carcinoma of the Tongue. Palmer Memorial Hospital.

WEDNESDAY, JUNE 14

Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Harvard School of Public Health, 55 Shattuck Street, Boston.

THURSDAY, JUNE 15

Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Harvard School of Public Health, 55 Shattuck Street, Boston.

FRIDAY, JUNE 16

Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Harvard School of Public Health, 55 Shattuck Street, Boston.

*10 a. m. - 12:30 p. m. Tumor Clinic. Boston Dispensary.

SATURDAY, JUNE 17

Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Harvard School of Public Health, 55 Shattuck Street, Boston.

Because of the holiday the usual staff rounds at the Peter Bent Brigham Hospital, conducted by Dr. Henry A. Christian, will be omitted.

*Open to the medical profession.

JUNE 9 and 10 — Seventieth Anniversary of the Children's Hospital. Page 976.

JUNE 12-16 — Catholic Hospital Association The Milwaukee Auditorium, Milwaukee, Wisconsin.

JUNE 12-17 — Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Page 815, issue of May 11.

JUNE 13 — Symposium on Carcinoma of the Tongue. Page 941, issue of June 1.

JUNE 20 — Lawrence Cancer Clinic. Notice above.

JUNE 26-29 — National Tuberculosis Association. Page 897, issue of May 25.

JUNE 27-29 — Medical Library Association. Page 941, issue of June 1.

JUNE 29 — Pentucket Association of Physicians, 8:30 p. m., Hotel Whittier, 5 Washington Street, Haverhill.

AUGUST 30 - SEPTEMBER 2 — Seminar in Physical Therapy. Page 857, issue of May 18.

SEPTEMBER — Boston Psychoanalytic Institute. Page 450, issue of September 22.

SEPTEMBER 4-6 — Institute for the Consideration of the Blood and Blood-Forming Organs. Page 941, issue of June 1.

SEPTEMBER 5-8 — American Congress of Physical Therapy. Page 857, issue of May 18.

SEPTEMBER 11-15 — American Congress on Obstetrics and Gynecology. Page 938, issue of December 8.

SEPTEMBER 14-16 — Biological Photographic Association. Page 941, issue of June 1.

SEPTEMBER 15-28 — Pan-Pacific Surgical Association. Page 863, issue of November 24.

OCTOBER 23 - NOVEMBER 3 — New York Academy of Medicine. Notice above.

FALL, 1939 — Temperature Symposium. Page 218, issue of February 2.

MAY 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

DISTRICT MEDICAL SOCIETY

NORFOLK SOUTH

JUNE 14 — Page 897, issue of May 25.

BOOKS RECEIVED FOR REVIEW

Clinical Pathological Gynecology. J. Thornwell Witherspoon. 400 pp. Philadelphia: Lea & Febiger, 1939. $6.50.

The Physiology and Pharmacology of the Pituitary Body. H. B. Van Dyke. Vol. 2. 402 pp. Chicago: The University of Chicago Press, 1939. $4.50.

What it Means to Be a Doctor. Dwight Anderson. 87 pp. New York: Public Relations Bureau, Medical Society of the State of New York, 1939. $1.00.

The Patient as a Person: A study of the social aspects of illness. G. Canby Robinson. 423 pp. New York: The Commonwealth Fund, 1939. $3.00.

Crystalline Enzymes: The chemistry of pepsin, trypsin, and bacteriophage. John H. Northrop. 176 pp. New York: Columbia University Press, 1939. $3.00.

L'Année Thérapeutique: Médications et procédés nouveaux. A. Ravina. 188 pp. Paris: Masson et Cie, 1939. 25 Fr. fr.

The Medical Press and Circular, 1839–1939: A hundred years in the life of a medical journal. Robert J. Rowlette. 127 pp. London: Medical Press and Circular, 1939. 10s. 6d.

A Textbook of Clinical Neurology with an Introduction to the History of Neurology. Israel S. Wechsler. Fourth edition, revised. 844 pp. Philadelphia and London: W. B. Saunders Co., 1939. $7.00.

Menstrual Disorders: Pathology, diagnosis and treatment. C. Frederic Fluhmann. 329 pp. Philadelphia and London: W. B. Saunders Co., 1939. $5.00.

Endocrinology in Modern Practice. William Wolf. Second edition, completely revised. 1077 pp. Philadelphia and London: W. B. Saunders Co., 1939. $10.00.

Medical Jurisprudence and Toxicology. William D. McNally. 386 pp. Philadelphia and London: W. B. Saunders Co., 1939. $3.75.

Health Officers' Manual: General information regarding the administrative and technical problems of the health officer. J. C. Geiger. 148 pp. Philadelphia and London: W. B. Saunders Co., 1939. $1.50.

Heart Patients: Their study and care. S. Calvin Smith. 166 pp. Philadelphia: Lea & Febiger, 1939. $2.00.

Laboratory Manual of the Massachusetts General Hospital. Francis T. Hunter. Third edition, thoroughly revised. 119 pp. Philadelphia: Lea & Febiger, 1939. $1.75.

BOOK REVIEWS

Roentgen Diagnosis of the Extremities and Spine. Albert B. Ferguson. 435 pp. New York: Paul B. Hoeber, Inc., 1939. $12.00.

From the Roentgenological Department of the New York Orthopaedic Hospital, under the authorship of its director, Dr. A. B. Ferguson, comes this valuable study of roentgen-ray technic and an interpretative discussion of the uses of the roentgen rays in the diagnosis of lesions in the spine and extremities. The keynotes of the study are the author's methods of analysis of the effects of trauma and disease on the various tissues involved in the osseous framework of the body: how these tissues react to inflammatory processes within or external to the bone; the distinctions that should be made between atrophy and decalcification, between cortical thickening and hypertrophy and between the different types of osseous density, that is, those caused by pyogenic agencies and syphilis or tuberculosis; and the characteristics that should enable one to distinguish a fracture line from congenital osseous defects that occur in the various bones of the body and the ways of distinguishing between calcification and ossification, all of which observations are helpful in differentiating pyogenic lesions from tumors, and so forth.

Calcifications occurring post-traumatically, after periosteal rupture and in the walls of bursas, also come in for discussion. In Chapter 3 is a consideration of decalcification, loss of structure and loss of substance, and how these defects are associated with the anemias, malacias, old-age atrophies, atrophies of disuse, Kümmell's disease, and so forth. In Chapter 4 the significance of soft-tissue swellings as indicative of already visible, nearby, osseous lesions, or such lesions not yet roentgenologically detectable but soon to appear, is discussed. Chapter 5 defines the pathognomonic indications of malignancy in diaphyseal bone, and in the following chapter the features that distinguish abnormalities of metaphyseal bone are considered, these peculiar features being due to the nature of the capillary circulation in the metaphysis and the fact that it is there that changes due to growth in bone take place. A chapter on the inherent disturbances of bone formation includes the chondrodystrophies, chondrodysplasias, achondroplasias, ostitis fibrosa, and so forth. The chapters on fractures and their healing contain much information in respect to the phases of callus formation and other matters of interest to those who deal with fracture repair. The development of the epiphyses and the occurrence of anomalous small-bone masses in various locations have a chapter devoted to their description. The final sections concern non-osseous tissues, — such as loose bodies in or about joints, — Charcot's disease and other degenerative lesions, bursal effusions, the arthritides, tuberculous and non-tuberculous lesions and lumbosacral anomalies.

The wealth of material on which the author could draw and the admirable reproduction of his more than 500 illustrations, supplemented, as these are, by 262 brief case histories from the hospital records, make this volume a most helpful guide to roentgen diagnosis.

Health at Fifty. Edited by William H. Robey. 299 pp. Cambridge: Harvard University Press, 1939. $3.00.

Among the agencies operating to promote the health of the people, the free public lectures delivered in Boston by the faculty of the Harvard Medical School hold high rank. Since the quality of these addresses warrants the widest possible distribution, twelve have been included in the book under the above-designated title.

In addition to the importance of having individuals know about the causes and effects of the commoner fatal and disabling diseases, a general appreciation of the economic and sociologic implications of them will bring about a more active co-operative spirit among intelligent and public-spirited laymen, which will promote progress in the health programs underway by organized medicine.

The subjects dealt with by these eminent specialists are heart disease, cancer, blood pressure, overweight and underweight, rheumatism, menstruation and the menopause, care of the eyes, vitamins, glands of internal secretion, the family medicine cabinet, mental health and the problems of old age. The writers have avoided the use of technical terms and have shown marked ability in presenting facts in an interesting and instructive manner. This volume should be in all circulating libraries, for the people who will profit most by reading it will not be among those who ordinarily frequent medical libraries.

Practitioners may well advise patients to read every chapter in the book during convalescent periods, when the mind is in a receptive mood. Other editions should follow this publication.